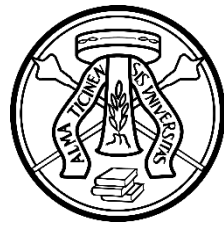


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The Impact of Ectogenesis on Human Relationships

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To my friends for always encourage me to continue and not give up.

And especially to myself, that despite the adverse conditions on a real and emotional level, I continued to try step by step, without even having any idea where this strength comes from.

Abstract

This dissertation thesis examines the perspective of Ectogenesis and the impact on human relationships. Special attention is given to parent-child relationships. Ectogenesis refers, to the technology which allows a fetus to develop independently from its mother's body. This technology will likely become a reality in the near future.

It is known that the first human relationship with another human being develops while being conceived in the womb. The bond between mother and fetus develops quite early during pregnancy and evolves continuously bringing neuropsychological changes to both members. The uterus is the environment in which the fetus develops, with the fetus actively participating and interacting with the environment. The way the fetus affects the pregnant woman and the synchronization between them both before and after its birth plays a decisive role. But what will happen in the case of an artificial womb? How will this impact the neuropsychological development of the fetus and child-parent relationship? The possibility of gestation ex utero is more than a mere extension of conventional preterm care and it marks a shift in physiological approach of the gestation procedure.

Here the term of gestateling will be used referring to the developing human being in an artificial womb. In this thesis it will be discussed how Artificial Womb Technology treats its subjects, in this case "gestatelings" and their moral status, the change in parent-child relationship, parent -clinician relationship, the psychological changes in the notion of parenthood, and the "psychological development of the fetus" social status.

PROLOGUE

This Master's thesis represents the culmination of my academic journey. It has been written to fulfil the requirements to obtain the master's degree in psychology, Neuroscience, and Human Sciences at the University of Pavia and IUSS. This thesis, titled "The Impact of Ectogenesis on Human Relationships" is presented to you based on the knowledge acquired during my academic studies and personal experiences.

I'm very grateful to my thesis supervisor, Dr. Andrea Lavazza, who allowed me to study a subject close to my heart for my Master's thesis. I deeply appreciate the opportunity. The allure of science does not only lie in meeting expectations but also in the unexpected, which allows us to uncover hidden dimensions of comprehension. The lack of immediate validation of hypotheses invites researchers to explore new paths, create new hypotheses, and drive toward deeper investigations. Ultimately, it is the desire to understand the world that gives science its genuine beauty. This experience has greatly enriched my perspective. As I anticipate the pursuit of a Ph.D., I am humbled by the depth of knowledge and experiences I have acquired during this journey.

This thesis project is divided into 3 sections. In the first introductory section, we establish the theoretical groundwork for our research. We discuss ectogenesis, its history and the current research. The second section of the thesis delves into the ethical arguments in favor of ectogenesis and the potential applications of ectogenesis. The third section describes the pregnancy and experiences of pregnancy. We explore antenatal attachment, attachment theory and the differences between maternal and paternal attachment. In addition, we discuss about the predictors of parent-fetal bonding during pregnancy and the links between the maternal-fetal tie and health practices during pregnancy. In this section we explore the psychological implications for the parental-fetus relationship and the psychological impact of ectogenesis on child and parent.

The last section lays out the discussion regarding the caregiving system and the influence of social support on the parental-fetal tie.

Chapter 1. Introduction

1.1. What is ectogenesis?

The technology that can make artificial human conception a reality will revolutionize reproduction, changing the fundamental tenet of human reproduction, that “a fetus must be carried in a woman’s body” (Bard, 2007). The artificial womb and ectogenesis will distract scientists from various fields. From 2017 to 2019 (Partridge et. al. 2017, Usuda et.al, 2019), research groups from the United States, Australia and Japan have published promising papers with results from tests on animals born from artificial wombs. Ongoing work in this area is making substantial progress towards the development of an artificial womb capable of facilitating the process of ectogenesis. Academic interest in the ethics of ectogenesis focuses on total ectogenesis. Ectogenesis refers to the artificial gestation or development of an organism outside the womb. It is a concept that involves growing embryos or fetuses in an artificial environment, typically in a laboratory setting, rather than within a natural biological womb. The term is often associated with advancements in reproductive technology and the potential to create an artificial womb for human gestation. Partial ectogenesis refers to the transfer of an embryo from a natural womb to an artificial womb for part of the pregnancy. Ectogenesis is an advanced alternative solution in the treatment of prematurity in newborns, as the latter is the leading cause of death in newborns worldwide (Ohuma et.al. 2023). Although neonatal intensive care units have evolved with modern equipment and incubators, mortality remains the same. Premature birth is the number one "killer" of children under 5, according to the World Health Organization. Because a baby's lungs and brain develop late in pregnancy, a child born prematurely is at risk for a lifetime of health problems. Premature birth also determines the increased probability of infant death (Perin et. al. 2022).

1.2. History of ectogenesis

The first interest on Artificial Womb technology appeared in the 19th century in the writings of Haldan, who used the term ectogenesis. From 1970 and for one decade, there was a discussion for the reproductive technology with the feminist approach focusing against of it. In 2000 the debate was reopened on how AW technology can provide a controlled environment for fetal development (Penge, 2006). Today the topic is more relevant than ever and recent animal studies, such as the EXTEND study and

the EVE study, are opening up the debate on human studies and moves closer towards clinical application in humans. (Patridge et.al. 2017, Usuda et. al. 2019). Both experimental studies succeeded in the development of animal lamb embryos in a sterile environment of an artificial wombs, with the technique of extracorporeal diffusion. (Romanis,2020, Tong, 2006).

Technique with donated wombs, bioengineered wombs technique, EXTEND research protocol and EVE research protocol

Ectogenesis can exist in different forms. Ectogenesis and the artificial womb do not overlap, and ectogenesis research may or may not involve tissue, or bioengineering technology.

The first in vitro culture of a human embryo was done only in 1988, it stayed in the uterus for 52 hours, and it came from a hysterectomy of a human uterus, from patients with cervical carcinoma or leiomyomas. Which was extracorporeally perfused with an oxygenated medium (Bulletti, et. al., 1998). This fact raises ethical dilemmas whether donated wombs can be used as an alternative to adoption and surrogacy in case of uterine factor infertility (Bulletti & Simon, 2019). The issues that arise concern, the consent agreement for the acquisition of the uterus, who can donate only patients or even healthy donors. In corresponding cases with uterus transplantations, similar issues have been addressed with the valid and informed consent of the donor (O' Donovan, et.al., 2019).

A variant of ectogenesis without the donor uterus is xenopregnancy, where an embryo or fetus is placed inside a uterine carrier belonging to a different species (Bulletti et. al., 2011). Which has been tested on animals. With this method there is the risk of immune rejection of the fetus, as well as the risk of transmission of infections between the carrier and the fetus. Concluding, the researchers aim at developing artificial wombs through tissue-engineering. (Vijayavenkataraman et. al., 2016, Hellström, et. al. 2020)

Organ tissue-engineering is method of creating organs analogous to native biological organs, by creating 3D scaffolds using biomaterials or by means of 3D bioprinting (Campo, et.al. 2017). Already attempts to produce organs like the bladder, lung, liver and vagina have been made (Campo, et.al. 2017). With the know-how that exists at this moment, the same will be done with the uterus, where they will have to reproduce its functions and the environment (Hellström, et. al. 2020).

The benefits of these studies (Hellström et. al., 2020) are in vitro research applications in endometrial cancer cells and drug screening applications as well as in vivo transplantation studies aimed at treating infertility (Hellström et. al., 2014).

According to Campo (2017) the aim of tissue reproduction through biotechnology is transplantation of the bioengineered uterus and not necessarily ectogenesis. Bulletti and Simon (2019) mentioned that in the future can be used for ectogenesis also. In this case issues concerning safety and proportionality, responsibility for fetal harm in case of malfunction, obtaining consent in case of use of donated cells as well as justification of animal testing and acceptance of use of human biological material, are some of the issues that arise.

The recent clinical studies that were successful in exogenous, were done with the use of sterile containers, where the embryo was transferred and not with the use of an artificial or bioengineered wombs (Miura, et. al., 2015). There are 2 ways to these techniques, using pumped driven or pumpless systems. Pump driven systems essentially control through the pump the drainage of blood into an oxygenator. Pumpless systems are arteriovenous and use the fetal heart to pump blood from the umbilical arteries (Bird, 2017).

Research has shown good results for both systems. In clinical animal studies the use of pump circuits for perfusion has been successful although for use in longer survival models with an extracorporeal a system without pumps is more successful (Bird, 2017).

In order for an Artificial uterus technology (AWT) to exist the blood circulation must mimic that of the uterus as it appears in the placenta with perfusion determined by the fetal cardiac output (Patridge & Flake 2020).

In 2017, a team of researchers from the University of Philadelphia developed an artificial womb, which carried a premature sheep to the end of pregnancy. The clinical trial was completed with the birth of a perfectly healthy sheep with the same results as a corresponding sheep born by natural delivery.

Developing the artificial womb, which was called a “bio-bag”, was a difficult process. A system had to be created to replace the processes that take place inside the uterus and the umbilical cord. The umbilical cord plays a crucial role in the transport of all nutrients for the development of the fetus, as well as the oxygenation of the internal organs of the fetus through blood transport, as well as the development of the lungs and respiratory system, a milestone for fetal viability. The “bio-bag” can safely support

the fetus for 4 weeks which helps to avoid problems related to the respiratory system of newborns. Other artificial womb attempts to date are EVE19 (Miura et.al.2015) and EXTEND20 (Hornick et. al. 2018). Both protocols refer to a biobag that reproduces the conditions of the womb, functions as a closed system into which the infant and amniotic fluid are introduced, and were performed in animals (Horn, 2022).

The protocol EXTEND was successful in supporting extremely preterm fetal lambs for 4 weeks without any apparent organ dysfunction or failure. The developing lambs were kept in a “biobag” containing continuously circulating synthetic amniotic fluid (Patridge et.al, 2017). In 2019 the EVE protocol was similarly able to maintain healthy fetal lambs for 5 days, with normal physical development, cardiovascular function and absence of infection or inflammation (Usuda, et.al. 2019).

Expertise in artificial womb technology has extended to the possibility of in vitro support of younger animals biologically comparable to a human fetus of 22-24 weeks gestation (Patridge et.al, 2017, Usuda, et.al. 2019) . It is reported that this will also be the primary clinical target population of the artificial womb as a life support platform for extremely premature infants, however if successful it will be extended to a longer gestation period and have more applications (Sahoo, et.al., 2019)

The University of Eindhoven has created dolls simulating premature babies and testing the effectiveness of the artificial womb (Solerte,2020).

1.3. Current Research – State of Art

Current scientific developments regarding reproductive technologies have developed extremely rapidly in recent decades. At this point the question is no longer whether to create an artificial womb or not, but clinical trials using human embryos. At 2023 FDA weighed the safety and efficacy of the devices, as well as ethical considerations for the first-in-human studies, and the results are expected. If the FDA gives its approval to test the "artificial womb" in newborns, its advisers want to assure that the device could actually facilitate development and reduce the rate of death and health problems in newborns, possibly compared to existing care offered in Neonatal Intensive Care Units (<https://www.fda.gov/media/172252/download>). The next 10 years probably the technology will be available in humans especially if there is a change in the guidelines for research in human embryos. At the moment research in human embryos cannot be extended more than 14 days, after the 14 days the material must be destroyed. If these ethical limitations are broadened that technology will soon be available.

Chapter 2. Ethical Arguments

2.1. Ethical Arguments in favor of ectogenesis

According to Singer and Wells (2006), ectogenesis in humans will offer significant advantages in topics such as surrogate motherhood, the improvement of neonatal care, the improvement of reproductive equality between men and women, the elimination of abortion, the increase of the population, the adoption of specific methods for purposes other than reproduction.

A) Medical benefit

Ectogenesis will enable women who have been subjected under a hysterectomy or women with a damaged uterus to give birth to a genetically related child of their own after ensuring they have stored their own eggs. The procedure will involve fertilized through in vitro fertilization and brought to term in an artificial womb. This procedure avoids the need for a surrogate mother either to carry the fetus or give her genetic material. Also, the need to adopt a child that is not genetically related to the mother., is eliminated. With this method prevention can be done more easily in relation to fertility and more options are given.

B) Solution to surrogacy problems

Issues arising from the solution of surrogacy are: difficulties in relation to the psychological and social well-being of the surrogate child, changes in the social constructions of the family that may have negative connotations, exploitation of the surrogate mother and concerns that pregnancy through surrogacy is tantamount baby buying and selling.

According to Murray (2001), the damage a child can suffer through surrogacy is very significant. In the case that the child becomes aware of the contract drawn up between the two parties, the surrogate child will discover that he was the subject of a commercial transaction and does not necessarily share 100% of the same genetic material with his parents, which will have psychological effects possibly disproportionate to the opportunity to exist in life. Also, the surrogacy method causes serious implications for basic family values and social constructions of what a family is. And it overturns the notion that "you can't choose your parents, nor can they choose you". This is overturned by the fact that there is control and choice in the process of conception.

Another big issue, is the exploitation of women who participate in the surrogate mother process. They usually come from lower socio-economic background and are vulnerable from financially strong families. Saravanan (2013), observed a cycle of exploitation among the intended parents, that surrogate mothers, the medical practitioners and the surrogate agents. In this cycle vicious of exploitation and power, the surrogate mothers are being the most vulnerable, however, even surrogate mothers through their remuneration and the knowledge they gain from the process enter into the process of exploiting the rest of the parties. The intended parents following the second position, due to their need for a child and lesser capacity, compared to the medical practitioners. Disproportions in power and authority lead to conditions where there is a lack of trust, and exploitation in human relations (Baier, 1994).

The last concern about surrogacy process is that it enhances the buying and selling of human beings as there is a price and contract with the processes. In this way human beings lose their inherent worth and gain price. According to Anderson (2000) the process of surrogacy commodifies women and children, and post-parental rights are treated as a property right in the market and the commodity is the children and not the service offered.

With these data it is understood that ectogenesis could be considered to be able to provide a solution to the problems of the surrogate process. According to the opinion of Murray the choice of a relationship undermines the person's commitment to it, the same happens with the surrogate process as parents have a choice or control over what characteristics their child will display so they are less committed to the relationship. But according to the example of adoption, where the adoptive parents choose the child they want to adopt, the above claim is not negated as it is not clear here that the choice threatens the person's sense of duty and obligation as a parent.

In the case of ectogenesis, the fact that the resulting child was conceived outside a woman's body does not undermine the obligation parents have towards their children, and the ability to choose continues to remain inherent in the ability to choose gametes and specifically to choose fertilized zygotes. Since ectogenesis offers an alternative to the use of a surrogate mother, it minimizes the risk of exploitation of the surrogate and commercialization of the child. So, it can be considered as a solution to surrogacy contracts.

C) Prematurity and mortality (neonatal care)

Addressing the prematurity of newborns is an important issue in relation to the increase in mortality. Premature infants are at risk of death due to their inability to take in food and absorb all the necessary components for their survival. They are also at risk of infections, unable to thermoregulate and have a vulnerable respiratory system. Premature babies do not have sufficient time to grow rapidly and master bodily functions which are critical to their survival. Technology related to the survival of newborns outside the womb includes intravenous feeding, cradles that regulate humidity and temperature, ventilators for breathing. Technologies that attempt to replace the functions of the missing womb, for the newborn to develop normally. According to Spencer and Wells, ectogenesis better addresses the alarming phenomenon of premature mortality, as the artificial womb better simulates the human womb.

2.2. Arguments against ectogenesis

Although artificial wombs and ectogenesis offer significant solutions to problems mentioned above also comes with ethical concerns about social implications, possible undesirable outcomes in terms of offspring welfare, and about whether regulation can keep up with the pace of the current developments.

The following arguments are analysed: A) the lack of appropriate human testing, on the claim that B) ectogenesis would be unnatural, and the argument that C) ectogenesis would lead to an ethically unacceptable slippery slope.

A) Human Testing

According to Singer and Wells the strongest argument to prohibit human ectogenesis is that this technology has not yet been tested on human subjects. The side effects would be unknown and also in many cases the body is irreplaceable and performs functions that cannot be imitated by the artificial womb and can potentially harm the others in the case the foetus. Although nowadays the technology is on this state of art before tested on human subject, similar to testing that was done in support of IVF or other reproductive technologies. Research is mostly concentrated on animals, like in any other new drug or technology and can serve as an essential link to potential human ectogenesis in the future.

It is true that the effects of certain drugs and technologies on humans can never be known until they are studied in trials, this is not a strong reason to oppose such advancements. It is difficult to argue that potentially saving technologies should be restricted until they are tested on humans and potential benefits and risks are known. Here there is a risk of never knowing the overall spectrum of the effectiveness and harmfulness. Ectogenesis is already tested and perfected on animal models to the point where it could be deemed safe to allow it to be introduced on a human population and could be beneficiary.

According to the precautionary principle that argues that “shifting the burden of proof in regulatory decisions from demonstration of harm to demonstration of safety of substances and practices.” (Stanford Encyclopedia of Philosophy). If we strictly follow the above principle there is no way to prove the safety of the new technology without using it on humans. The intention of the precautionary principle is to ensure the safety of the public and the environment which makes new technologies very difficult, although in times of crisis some rules can be overridden, like in the case of COVID. Taking into account, the example of the first IVF in 1978, the associated predictions of possible harm were wrong and all they did was provoke a series of critical reactions from various scientific groups. The prediction was that would follow terrible consequences for the parents, the child and society. But nowadays many children are born in vitro fertilization, with none of the consequences that were mentioned.

B) Unnatural procedure

One can argue that the use of artificial wombs and ectogenesis is an unnatural process compared to the physical pregnancies, and therefore normal pregnancies are supported over ectogenesis. According to Singer and Wells this doesn't mean that natural is a good thing and unnatural is a bad thing, especially if it is taken into account the fact that a lot of times in nature “bad things” occur like tumors, diseases. So ectogenesis based on the unnaturalness argument is insufficient.

C) Slippery slope

Another important argument against ectogenesis is the fear of a start of slippery slope that leads into farming human in the laboratory. In this case human life would be devalued and people will be produced according to political, economical, scientific

needs, similar to commercial animal farming. Human life would become dispensable and will lose its inherent value. If this argument is valid, that means that the ability to choose and the ability to control human life will lead to disastrous outcomes (Singer&Wells, 2006). However, if human ectogenesis were to be implemented, legal guidelines and restrictions would be applied in order to ensure that human life would be commercialized and farmed. Guidelines and regulations can ensure that the technology was not misused. These guidelines must be under constant checking and modification, when needed, in order to ensure the process in the human setting. With these opposes arguments it can be concluded that ectogenesis could be regulated like other reproductive technologies.

Principles of choice and control, give more choices regarding the continuation of life rather than undermining and devaluating the value of life. Adaption is a characteristic example of the principles of choice and control over the reproduction, and the various options that are created. Potential parents can choose the age of the child, sex, background, origins. At the same time new opportunities are created for the adapted child in order to have a family.

2.3. Potential applications of ectogenesis

Ectogenesis as a solution for neonatal care in prematurity

Although research on human fetuses has not yet begun, the ultimate goal of the method is to provide the fetus with an environment that can grow, mimics the womb, and does not have the pressure of premature birth. The aim is to improve existing neonatal care systems for extremely premature infants, reducing morbidity and mortality in existing neonatal intensive care units (Bird, 2017). Existing ventilation-based life support technology has a limit to effectiveness, as the pulmonary immaturity of premature fetuses does not keep pace with pulmonary gas exchange in the lungs (Partridge, et.al., 2017).

To the extent that this technology will be able to be more effective than existing technologies for premature infants remains to be proven (Romanis, 2018). However, progress is also accompanied by concerns about social implications and the undesirable outcomes on the well-being of offspring.

The extent to which the artificial womb can replace or continue existing neonatal intensive care is under debate. Romanis (2018), differentiates the neonatal intensive

care unit from the artificial womb, on the basis that the subjects of the ectopic pregnancy are unique human entities which she terms as “gestatelings”.

The experimental use of the artificial womb AWT in premature infants will create pressure on prospective parents to consent to experimental procedures. According to Partridge (2017) and Usuda (2019) partial ectogenesis is not intended as an alternative solution to complete ectogenesis but as an improvement of neonatal care. On current data, partial ectogenesis will be completed before full ectogenesis (Romanis, 2020). Partial ectogenesis affects the pregnant woman as the fetus is removed from the uterus and placed in the artificial wombs (Romanis, 2020).

An incision is made in the uterus—resembling a Caesarean—to expose the fetus, after which it is transferred to the sterilized container (Partridge, et.al. (2017), Usuda, et.al. (2019)). It is likely that this intervention will be no less risky than a Caesarean section—with the potential to be significantly riskier.

C-sections are known to carry risks such as blood clots, uncontrollable bleeding and an increased risk of other obstetric complications (e.g. heightened risks of hysterectomy, abnormal placentation, uterine rupture) (Segers, et.a.l, 2020).

Kingma and Finn (2020) recently hypothesized that some of these risks are more likely after partial ectogenesis (as the uterine incision will be done at an early pregnancy stage, when uterus is less stressed, the scar from one pregnancy is larger and increases the risks of uterine prolapse and placental implantation problems, so ectogenesis will develop a new field in fetal medicine.

Advancing fetal medicine and optimizing the fetal environment

According to the literature, the treatment of the fetus is easier when it is done extrauterine (Kendal, 2017). However, when it becomes intrauterine, it involves risks for the pregnant woman and complications such as uterine rupture (Smajdor, 2011). however, although partial exogenous treatment could make possible the extrauterine treatment of the fetus, its transfer to the external uterus is a complicated procedure that requires surgery. (Segers et.al., 2020).

Concerns for the physical well-being of the pregnant woman is important, and existing neonatal care guidelines urge pregnant women to medical intervention for the benefit of fetal viability. New technology can amplify these pressures for intervention (Segers et.al., 2020).

In the Usuda et. al. (2019) clinical study it is still unlikely that fetuses under 20 weeks of gestation, will be able to survive in an artificial placenta as catheterization of the umbilical vessels endangers the function of the fetus's heart.

The expected benefit of ectogenesis in relation to the well-being of the fetus, concerns the optimization of the environment of the fetus, in relation to its nutrition, its temperature, its oxygenation. The idea of a safer womb puts pressure on expectant mothers to take interventions for the benefit of the future child (Romanis, 2020).

This can happen when there are people with delinquent behaviors, the use of substances that endanger the life of the infant (Romanis, 2020). Greater knowledge of what happens in a pregnancy through ectogenesis could bring greater control over normal pregnancies (Takala, 2009). In the event that ectogenesis has better outcomes in relation to maternal mortality and morbidity, this will endanger the natural pregnancy absent the control of pregnancy parameters (Sahoo et.al., 2019). Ectogenesis could therefore alter the meaning people find in gestation and childbirth, creating a conflict between wellbeing of the future child and autonomy of the pregnant person (Cavaliere, 2020).

For disadvantaged populations, the use of ectogenesis may lead to increased pressure for use, for the sake of fetal safety and survival. Here the concept of free choice and freedom in general in relation to the use of the artificial womb seems to be affected.

As Cavaliere (2020) mentions, that disadvantaged women are in additional risk, because may be viewed as “substandard gestators” compared to AWT, which might enhance existing social inequalities. Finally, according to Tong and Murphy the possibility to scientifically control the fetal growth environment might, increase the striving for ideal fetuses in ideal milieus (Sahoo, et.al. 2019). A related topic that receives relatively little attention is how ectogenesis could make genome editing easier in fetuses, both for disease related and non-disease related traits (Rowland, 1987). Issues relating to equality, justice and disability discrimination also seem not to be covered by ectogenesis (Segers & Merter, 2020).

Chapter 3

3.1. Pregnancy and experiences of pregnancy

For the past 50 years, the science of developmental psychology has emphasized the relationship that is formed between parents and their fetuses (Alhusen, 2008). During

pregnancy, parents-to-be, and especially mothers-to-be, develop a degree of connection and emotional attachment to the fetus (Doan & Zimmerman, 2003; Lawson & Turriff-Jonasson, 2006). The quality of fetal attachment is determined by many risk and protective factors (Bouchard, 2011). The mode of conception and the environment of pregnancy are important factors.

The psycho-emotional and cognitive development of the child is affected by prenatal parent-fetal attachment. Parent -fetal attachment is associated with parental self-care behaviors during pregnancy and commitment to practice healthy behaviors for the sake of the fetus (Van den Bergh and Simons, 2009). Prenatal attachment refers to how each parent creates mental representations of the child, uncomplicated by the infant's temperament and early parenting experiences.

3.2. Antenatal Attachment

Cranley (1981) first mentioned the concept of maternal-fetal attachment and defined it as the degree to which pregnant mothers engage in attachment and interaction behaviors with the fetus. The concept has been criticized because it focuses on the behavioral aspect of bonding mainly, without being able to reveal the extent of parental perceptions (Doan & Zimmerman, 2003).

According to Müller (1993) parental- fetus attachment gradually develops over pregnancy and significant parameters affect the ability of the parent to form this attachment. Like parent's early childhood influences, particularly the mother's attachment to her own mother, on her ability to form relationships with others, including the unborn child.

Antenatal attachment is defined as the emotional tie developed between the mother and the fetus (Condon & Corkindale, 1997). The specific definition refers to the parent who carries the child, particularly the mother. It was suggested that the emotional tie develops in concert with increasingly elaborate internalized mental representations of the unborn child.

Other researchers suggested that Parent – Fetus Attachment (PFA) depending on the feeling of protection and not of love, which will occur after birth (Sandbrook & Adamson-Macedo, 2004). Fear of fetal loss in the early gestational period, has a strong influence in the progression of PFA. The extent of support received from partners and other family members, can strengthen the maternal instinct to protect, and provides

motivation for changes in behavior that encourage fetal wellbeing (Sandbrook and Adamson-Macedo, 2004).

Doan and Zimmerman (2003), mentioned that the emotional relationship between parent and fetus, is present before pregnancy, and the ability of emotional and cognitive conceptualizations about another human being, is strongly related to capacity to formulate relationships, and the relationship itself. Like any other ecological system that each member affect the system in its unique way.

They mention that the parent's identity and experiences before the pregnancy are likely, through ongoing developmental patterns, to influence expectant parents' ability to form an attachment to the unborn child.

They propose qualities that may aid the development of antenatal attachment, such as secure attachment to one's parents, the cognitive ability to conceptualize and internalize the representation of the fetus, and the intention to sensitivity and reciprocity towards fetal conceptualizations.

Other suggested that there are three critical contributing attributes of MFA. These are cognitive attachment, the desire to know and understand the baby. This comprises visualization of the unborn child through fantasy and conceptualization, as well as the assignment of characteristics to the fetus. Affective attachment describes the pleasure related to thoughts about the fetus, the interactions with the fetus. An example of an interaction is the gratifying experience of fetal movement sensation. And finally, the desire to protect the fetus, along with physical preparation for the infant's arrival, is called altruistic attachment. This attribute includes maternal behavior that shows concern for the baby's health.

According to Bowlby's theory (1969) of attachment, early attachment relationships are formulated through representational models of the relationship. Representational models are about conceptions about the environment and the individuals within it. These conceptions imprint the formulation of social relationships and their stability. The antenatal relationship is unidirectional and consists of the cognitive and emotional reactions of the parent towards the fetus (Redshaw & Martin, 2013).

According to these findings the tie between parents and the fetus is a multi-faceted construct and must be more affected by the caregiving system (Redshaw and Martin, 2013).

3.3. Attachment Theory (a. introduction, b. measurement, c. differences between maternal and paternal attachment)

3.3.a. Introduction

According to the attachment theory the prenatal or fetal bond is described as the bond that develops between future parents and the fetus (Laxton-Kane & Slade, 2002; Walsh, 2010). The principles of attachment try to explain how future parents try to get to know the fetus, feel closeness, protect and satisfy its needs (Laxton-Kane & Slade, 2002).

Attachment theory (Bowlby, 1950), explains that attachment relationships with primary caregivers from infancy and onwards are of utmost importance for the healthy psycho-emotional development of the person and their subsequent functioning. (Cassidy, 2008; van Ijzendoorn & Sagi-Schwartz, 2008). Especially in emotion regulation, social functioning and cognitive development. Attachment theory assumes that all human beings are dependent on others, and try to regulate their emotions through relationships. This applies across the life-span (Mikulincer and Shaver, 2008). The attachment bond differs from other emotional bonds, as it includes a certain basic criterion this criterion is that the person seeks relief, protection and security from this relationship (Bowlby, 1969, Ainsworth, 1989). Thus Bowlby (1969) stated that the term attachment can be used to describe the relationship from the child to the parent and not the other way around (Cassidy, 2008). Under normal circumstances parents do not seek security in their children (Bowlby, 1969). So, attachment refers to care seeking rather than care giving (Walsh, 2010). The developing tie between a mother and the fetus is unique, but this relationship is not equal between the two members, and must be taken into account (Van den Bergh and Simons, 2009; Walsh, 2010).

3.3.b. Measurement of perinatal attachment

According to Bowlby (1958) infants have an innate drive to maintain psychological closeness to the primary caregiver. Common attachment behaviors occur when infants feel threatened. The threat can be pain, hunger or the presence of a stranger. The quality of the infant-caregiver attachment bond is assessed by the caregiver's availability in stressful situations. Availability of care is determined by his personality traits and patterns of interaction that have developed over time (Weinfield et al., 2008). In this point, it must be taken into account that in parent-fetus relationship is very difficult to examine the fetal part of the relationship during pregnancy. What is essentially studied and evaluated during pregnancy are one-sided cognitive, emotional

processes of the parents, and particularly that of the mother, who gestates (Wilson et al., 2000). However, it is argued that technological advances such as fetal imaging allow parents to relate to the unborn and create a framework of reciprocity (Brandon et al., 2009)

According to Attachment theory, prenatal attachment can be measured with tools that investigate the attitudes and perceptions of future parents. However, measurements are imprecise given the complexity and inter-individual variability this is because, it may be that what existing tools are measuring does not accurately represent parental understandings of their tie to the fetus, or that the PFT does not lend itself to accurate measurement through self-report measures, given its complexity, and the variability between individuals (Van den Bergh & Simons, 2009).

3.3.c. Parental attachment (differences among mothers and fathers)

Bowlby (1969) suggested that most infants form an attachment to multiple caregivers. Nowadays, there is more than one attachment figure, that of the father (Cassidy, 2008), even though in many cultural contexts men spend less time caring for their infant than do women (van Ijzendoorn & Sagi-Schwartz, 2008). Both parents have been identified as playing an important role in the longitudinal developmental achievement of attachment security, or insecurity, in their children (Grossman et al., 2008).

However, in relation to the prenatal bond, some believe that only the mother can talk about physical contact with the unborn child and the bond with the father exists mainly on a conceptual level. The tools used so far to measure prenatal bonding with the father are the same with the ones' used for the mother, simply worded with a gender perspective, obviously other conceptual frameworks and tools for the father are needed (Armstrong, 2000).

3.4. Predictors of parent-fetal bonding during pregnancy

3.4.a. Development of the parental-fetal tie during pregnancy

As the pregnancy progresses, so does the bond between the fetus and the parents (Gioia, et. al. 2022). Research has shown that the month of pregnancy is a more reliable predictor for the progression of the bond between mother and fetus (Yarcheski et al. 2009). Also, the presence of fetal movements increases the sense of attachment, which

reinforces the maternal sense that the infant exists (Laxton-Kane & Slade, 2002). Parent-fetal bonding is a predictor of postnatal bonding for both parents. In women the bond that develops during pregnancy is a precursor to maternal attachment to the infant after birth (Hjelmstedt & Collins, 2008). Attachment is a crucial factor in the physical, cognitive and emotional development of the fetus (Siddiqui & Hagglof, 2000). Cordon et al. (2008) states that the attachment of a parent to the infant does not result from the interaction with the infant but from the parent's inherent ability to form bonds, the ability of the parent to create mental representations of the fetus affects in a positive way, the formation of a bond with the fetus and with the infant later on (Theran et al., 2005).

Lack of attachment to the fetus can have negative effects on fetal development and subsequent parenting behavior. The growth of the parents-fetus bond, strengthens the maternal sensitivity, the participation of the parents in the care of the infant. Also the parents' thoughts and emotions about the fetus during the gestational period enhance the development of attachment after birth. (McMahon et al., 2017)

3.4.b. Links between the maternal-fetal tie and health practices during pregnancy

Indicators of the parents-fetus bond are the health and self-care behaviors adopted during pregnancy by parents and especially mothers (Van den Bergh & Simons, 2009). High correlation was found between health practices and the development of the maternal bond. It was observed to be high among women living in cities and of low economic income (Alhusen et al., 2008). In smoking parents, number of cigarettes consumed moderated the association (Magee et al., 2014). Mothers with evidence of depression showed lower fetal bonding and prenatal attachment (McFarland et al., 2011). The degree to which parents feel connected to the fetus appears to influence engagement in health behaviors, higher engagement is related to higher fetal awareness.

3.5. Psychological Implications for the parental -fetus relationship

3.5.a. Research on psychological impact on children conceived by ART

Studies that were done on children who were conceived from IVF treatment compared to those that were conceived naturally, found that IVF children (from 9 to 18 years

old) scored higher in the borderline/clinical range on depressed behavior (Wagenaar et al. 2009). In a systematic review analysis on the long-term consequences of birth from IVF treatment, there was an increase in the prevalence in early adulthood of clinical depression, attention-deficit disorder and binge drinking on IVF born children (Hart & Norman, 2013). Another study suggested that children born with Assisted Reproductive Technologies are at greater risk to develop autism, due to advanced age of parents (Zhan et al, 2013). Golombok et al. (2009) conducted a study in 18 years old adolescents conceived by in vitro fertilization, about psychological well-being and parent-child relationship. The results showed that this group have lower self-esteem than the naturally conceived group.

Significant differences also found between Assisted Reproductive Technologies (ART) born children and naturally conceived children. The rate of hospital admissions was measured before the children became 9 months old. The ART group showed higher rates, although beyond 9 months had a good prognosis regarding health and well-being (Sutcliffe et al, 2014). Murray et al. (2006) studied egg donation, donor insemination, and IVF families in 12-years-old children. They found that egg donation children showed no evidence of psychological problems and there were no significant differences between the egg donation families and IVF families.

In comparative studies between surrogacy, egg donation, donor insemination and natural conception families on parenting and children's adjustment found that children born through Reproductive Donation obtained normal results regarding the strengths and difficulties in adjustment (Golombok et al, 2017). In the follow-up study at age 14 there were no differences between any group, for adjustment problems, psychological well-being, and self-esteem (Golombok et al., 2017).

Difficulties with interpreting the results in these studies have to do with the evaluation measurements and sample size, cultural differences and under-report child's difficulties especially in reproductive donation mothers who give more positive attributes to children's behaviors (Golombok et al, 2017).

3.5.b. Research on ART mode of conception and psychological impact on parent attachment style

In cases of pregnancy with embryo donation, it is observed that the mode of conception can affect the quality of parenting (Laxton-Kane & Slade, 2002). In recent years the

concept of prenatal mother-infant attachment has been linked to postnatal infant attachment styles. (Muller, 1996)

Assisted Reproduction Therapies can affect parenting attachment style. In the cases of infertility emotional stress can lead to dysfunctional parenting behaviors. Also the child acquires the concept of being valuable resulting in overprotective and intrusive parental behaviors (Hann&DiPietro,2001). Emotional over involved parents, can cause problems in the psycho-emotional development of their children as the development of autonomy is delayed and stress levels increase (Hullmann, et. al. 2010).

Studies have shown that IVF and embryo donation parents have a tendency to over protectiveness and over involvement parenting but overall good parent-child relationships, these results are explained due to the history of low infertility (Golombok et al., 2002).

Defensive responding is another measure of psychological impact on attachment parent style. Defensive responding refers to the disinclination of reporting negative feelings about parenting. For IVF parents the defensive responding was high and was correlated with the number of failed fertility cycles. Higher number of failed cycles indicated higher levels of defensive responding. (McMahon, et. al., 2003). The same results found for embryo donation parents. Defensive responding is a trait that shows low levels of communications and awareness within a family. Characteristics that are common in abusive and non-communicative families.

In studies examining the relationship of the gestational link to positive parenting among embryo donation and adoptive families, it was found that the surrogate's psycho-emotional state affects the welfare of the fetus. Surrogate's stress levels can carry harmful inherent factors that affect the development of the fetus. Also lack of acceptance and recognition by the surrogate can act harmfully on the fetus. through epigenetics cells are transferred between the fetus and the mother through the placenta, antibodies and nutrients are transferred (Burrell et. al., 2014).

During the period of gestation until the period of breastfeeding, the fetal consciousness develops. In this period there are many physical, emotional and environmental signals that affect the development of the fetus. A stimulus could be maternal acceptance or rejection which can be imprinted as a stimulus in the human cells. Research has shown that adrenaline, which is activated when there is stress, passes from the mother's blood

to the placenta and then to the fetal blood, causing the fetal's heart to beat faster and the breathing to accelerate (Huffman et. al. 1990).

On positive aspect on ART mode of conception is that is protective over maternal complications and fetal abnormalities. The rate of maternal complications and fetal abnormalities were measured among surrogate and natural pregnancies and higher rates were found in normal pregnancies than in pregnancies with artificial means or via surrogacy. This is due to the extensive obstetric control and the thorough investigation of the history of the surrogate mothers as well as the previous history of healthy pregnancies. In natural conception all the prerequisites are not fulfilled, and although there is higher risk for complications during surrogacy cycles, success rates still remain higher in relation to natural pregnancies (Dar et al., 2015).

3.5.c. Psychological impact of ectogenesis on child and parent

The potential impact of ectogenesis on children born through it, brings concerns about how harmful it can be. The first concern about ectogenesis was manifested 100 years before, and it was claimed that natural pregnancy was necessary more for children than for mothers (Brittain 1929, Tong et.al. 2006). The researchers Singer and Wells (1984) have brought back this concern about how harmful ectogenesis can be to children.

The psycho-emotional development of the child remains on research focus, although in recent years emphasis has been placed on how the relationship between parent and child is structured, and what is the psychological impact on the adult, who will not have the sensory experience of pregnancy, in the case of ectogenesis.

According to Sanders-Straudt (2006), the use of the artificial womb can lead to an increased psychosomatic distance between mothers and fetuses, as a result of which the social development in the course of the child's life will be affected. Pregnant women develop a relationship through physical stimuli they receive from the fetus. A movement from the fetus can cause feelings in the mother and vice versa. Mothers sing or speak to fetuses. The processing of contractions and milk flow as a result of psychosomatic sensations has also been observed.

So far it is known that the pregnant woman's oxytocin levels significantly promote the expression of maternal behavior after birth (Brunton&Russel, 2010). In relation to UTx the physical sensation of pregnancy plays an important role in the development of the bond between child and mother. This argument for UTx is used despite the absence of pelvic nerve connections (Segers et.al., 2022, Caplan, 2020, Orentlicher,

2017). Golombok (2017) reported that the absence of a pregnancy bond between child and parents does not seem to significantly affect children's psychological development and parents' psychological well-being. Studies about the relationship between adoptive parents and adoptive children appear to be able to replace the dependence of maternal bonding on natural pregnancy (Smajdor, 2007).

Of course, the above studies refer to children who have been conceived by someone, not by their parent but by another human being, while ectogenesis refers to the absence of human conception and gestation (Steiger, 2010). It is therefore difficult to predict what will be the impact on the psychological state of these children and how they will develop in the environment of the artificial womb. Sanders and Strauss argue that if the stimuli received by fetuses in the womb, which form the basis for feelings of affection and intimacy with another human being, are lost, this will have very serious psychological consequences (Sander-Straudt, 2006).

According to perinatal psychology, a child's psychological development begins from conception in the womb, where there are the stimuli of the parents' voice, the mother's heartbeat, the parental touch, mother's emotions and hormonal influence (Schoberer et al. 2012). All of these affect the neuropsychological development of the fetus. One of the changes that ectogenesis will bring is more opportunities for the fetus to interact with the father.

In order for a successful ectogenesis to occur, research should be able to simulate other features of natural pregnancy beyond nutrition, breathing, and waste removal (Sander-Straudt, 2006). This seems difficult, as simulations are currently done in animal models (Schoberer et al. 2012). As far as the human models are concerned, the research should continue until the birth of the child in order to draw safe conclusions and to be able to assess the risk of psychological damage (Singer&Wells, 2006). Further research should focus on longitudinal studies.

3.4. Caregiving System (variance and caregiving behaviour)

Influence of social support on the parental-fetal tie

Social support is an important social factor for the smooth transition of the parent to parenthood and the development of the bond with the fetus (Balaji et al.,

2007). Research on vulnerable populations such as teenage mothers, low socio - economic status, vulnerable groups showed that social support can enhance the development of the bond between parents and fetuses (Alhusen et al., 2012a, Maas et al., 2014)

Results in non-vulnerable populations showed less variability relative to attachment and social support (Maas et al., 2014). This may be due to the fact that there may already have social support from various parties, such as from family, intimate partner social environment.

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