The Formation of the Maternal–Fetal Relationship

A Reflection on the Findings of Modern Medicine

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Abstract. Previously conducted research has determined that physiological and psychophysiological communications evident during pregnancy are vital to the bond formed prenatally. These innate biological responses are further enhanced through psychophysiological factors, such as maternal prenatal stress, which attest to the essential communication between a mother and child in maternal–fetal attachment. A consideration of these factors is necessary with the increase in assisted reproductive technology, such as in vitro fertilization, surrogacy, and elective cesarean section, as this may affect the development of the maternal–fetal bond. It would be of benefit to the child, the mother, and every society to seek a more complete understanding of the intricate maternal–fetal bond, as the first friendship developed at the beginning of human life.
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For each person, there exists a deep and abiding need for friendship, a desire to love and be loved in return. Even in the event of success, riches, and gains, it has been suggested that a life without true friendship, without the bonds formed in mutual and recognized love, is a life not worth living. The mutual goodwill and self-giving cherished between lovers, between a child and parents, between friends formed in our neighborhoods, in our nations, and even worldwide, serves to save our souls from

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the greatest of losses.[1] In the midst of the many sufferings and tragedies of our world, friendship is among the greatest treasures mankind can share. In our times, a gaping sense of the loss of friendship has permeated our society. In the United States alone, reports have shown that the majority of the population feels a deep loss, with a declining sense of friendship and community. As Blessed Mother Theresa eloquently stated, "The greatest suffering is to feel alone, unwanted, unloved. The greatest suffering is also having no one, forgetting what an intimate, truly human relationship is."[2] Yet as many social projects are carried out to ease the sufferings of the physically impoverished, few targeted intellectual and social efforts are currently employed to seek solutions for a poverty that is no less important for the well-being of every human being.

There do exist modern movements that seek to make societal conditions possible for friendships, albeit often implicitly. Within the discipline of medicine, great lengths have been taken to improve the care and well-being of the patient. Doctor–patient relationships have improved, greater knowledge and use of advanced technology have led to better health outcomes and quality of living, and increased efforts have focused on the essential respect and dignity due to each human being. These and other improved conditions of well-being and health make possible the development of friendships, as only in a state of health can one pursue such good.

One subspecialty of medicine, that of maternal–fetal medicine, may be part of the solution to the loss of friendship by examining the form of attachment and type of friendship developed through love and self-giving between a mother and child. The maternal–fetal bonds are the core of the family, the "nucleus" of society, and the earliest, and arguably the most important, influence in our friendships. Therefore, by studying previously conducted research, the earliest form of attachment in a human's life will be explored—namely, that of maternal–fetal relationship during pregnancy—by examining the physiological and psychophysiological communications between a mother and child.

Attachment Theory and the Maternal–Fetal Attachment

Early attachment theory was developed by the psychologist John Bowlby. He proposed that the early child–caregiver attachment, which is most often a mother–child attachment, reflects the quality of the child's interpersonal relationships throughout life. Meta-analysis studies performed to determine if this theory could be supported connected early attachment to the development of bonds and friendships throughout the participants' lives. Significant results were found for the predictive power of the attachment theory. Remarkably, results for one of these studies indicated that attachment was more important for friendships than other interpersonal bonds.[3]

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[1] Aristotle, *Nicomachean Ethics*, book 8, trans. Roger Crisp (Cambridge: Cambridge University Press, 2000).

[2] José Luis Gonzalez-Balado, *Mother Teresa: In My Own Words* (New York: Gramercy Books, 1997), 91.

[3] See Susanna Pallini et al., "Early Child–Parent Attachment and Peer Relations: A Meta-analysis of Recent Research," *Journal of Family Psychology* 28.1 (February 2014): 118–123.

The possibilities presented in studying the attachment theory and its subsequent mental and physical health, functioning as an adult, and health-related behaviors have been extended to medical practices, patient–physician relationships, and overall health care. Attachment theory has been used to enhance health-related communication and behaviors in patient care, including therapeutic contexts.[4] The study of attachment theory can be further extended to maternal–fetal attachment and the communications essential to this bond, to better understand and implement care, particularly for the child's well-being and development throughout life.

Preparation for Maternal–Fetal Attachment and the Maternal-to-Zygotic Transition

Even before the moment of conception, the mother's body has been shown to prepare for the child through the presence of the gametes in the oviduct of the mother's reproductive system. At this pre-fetal stage, the intricate workings of the maternal–fetal relationship have begun to develop. In a study performed by Alireza Fazeli et al., an oviduct organ culture demonstrated that the presence of either of the gametes serves to alter the protein secretions of the oviduct.[5] The spermatozoa produced a specific response and may induce de novo protein synthesis in the epithelial cell of the oviduct, while oocytes induced oviductal gene expression.[6] Both gametes altered the protein secretions within the oviduct, developing the microenvironment in which a pregnancy can occur. Further studies by Stephen Georgiou et al. have shown that the presence of the sperm and oocyte altered the oviductal gene expression, beginning the local, immediate control of the microenvironment for the filial development as part of this gamete recognition system.[7] This demonstrates that the maternal communication with the embryo initiates before conception, to prepare future stages of this complex interaction.

After conception, the maternal–fetal interaction continues at the genetic level, through the maternal-to-zygotic transition (MZT). All animals experience a stage in which development passes from the control of the maternal genome to that of the zygotic genome. The maternal mRNAs (messenger ribonucleic acids) and proteins initially direct the biosynthetic processes, mitotic divisions, and cell fate and patterning in the fetus. The first elimination of maternal mRNAs and the transcription of the zygotic genome then trigger the start of MZT. Further enhancing the intricate workings of this process, the maternal and fetal genomes continue to promote the MZT through exchanged physiological communications. The zygotic transcription produces proteins and mRNAs to increase the efficiency of maternal mRNA degradation, while the early maternal mRNAs include transcriptional activators to improve

[4] Lisa M. Hooper et al., "Using Attachment Theory in Medical Settings: Implications for Primary Care Physicians," *Journal of Mental Health* 21.1 (February 2001): 23–37.

[5] Alireza Fazeli et al., "Maternal Communication with Gametes and Embryos: A Complex Interactome," *Briefings in Functional Genomics and Proteomics* 7.2 (March 2008): 111–118.

[6] Ibid.

[7] A. Stephen Georgiou et al., "Gametes Alter the Oviductal Secretory Proteome," *Molecular and Cellular Proteomics* 4.11 (November 2005): 1785–1796.

zygotic transcription.[8] This communication at the most intricate of levels serves to further enhance the maternal–fetal bond at an early stage in pregnancy.

The Prenatal Hormonal Environment and Maternal–Fetal Attachment

Several neuro-endocrinological factors also serve to facilitate the biological responses of maternal–fetal attachment that develop during pregnancy, including prominent hormones such as vasopressin, noradrenaline, and cortisol. For vaginal birth, the newborn experiences extremely high levels of vasopressin, a hormone secreted by cells of the hypothalamic nuclei and stored in the posterior pituitary. In the study performed by Yael Apter-Levi et al., predictors of vasopressin included stimulatory contact, joint parental–child attention, and an increase in maternal object salience as a response to the newborn gaze.[9] Noradrenaline, a hormone and neurotransmitter, which increases in concentration in the fetus during parturition (childbirth), has a positive correlation with olfactory learning in a newborn child. As the maternal odor is the first biologically relevant odor for the newborn, the increase of noradrenaline during pregnancy may contribute to the maternal–fetal bond.

Similarly, the steroid (glucocorticoid) hormone cortisol has levels in human mothers that have shown a positive correlation with maternal behavior, such as a recognition and attraction to baby odors. For the child, the pressure during parturition causes the enhanced release of physiological factors, including cortisol. The increased serum cortisol levels have been hypothesized to be a necessary primer for the extra-uterine life.[10] In addition, as cortisol can cross the placenta, both the mother and child can be affected by the changes in this hormone, responding to the biochemistry in communion. Each of these biological factors plays a role in the maternal–fetal relationship, strengthening the complex bond formed.

An additional component in the physiology of pregnancy is the neuropeptide oxytocin, an essential factor in human interactions. Oxytocin, the "social hormone," is enhanced by social interactions and in turn works to form the biological basis of community bonds, particularly with immediate family and loved ones. Although the majority of findings involve maternal bonding in other mammals, several studies have demonstrated that humans also benefit from the effects of oxytocin. A study conducted by Madelon Riem et al. demonstrated that oxytocin can improve pro-social behavior through brain networks, specifically changing the connectivity between the posterior cingulate cortex and the brainstem to improve social behaviors.[11] These complex brain networks are involved in affectionate touch and self-referential processing, and in

[8] Wael Tadros et al., "The Maternal-to-Zygotic Transition: A Play in Two Acts," *Development* 136.18 (September 2009): 3033–3042.

[9] Yael Apter-Levi et al., "Oxytocin and Vasopressin Support Distinct Configurations of Social Synchrony," *Brain Research* 1580.11 (September 2014): 124–132.

[10] Ibid.

[11] Madelon M.E. Riem et al., "Oxytocin Effects on Complex Brain Networks Are Moderated by Experiences of Maternal Love Withdrawal," *European Neuropsychopharmacology* 23.10 (October 2013): 1288–1295.

this study were most prominent in individuals with supportive families. Additional brain regions, such as the insula and inferior frontal gyrus, are related to oxytocin and the increased activation of the emotional processing during social stimuli. Further studies using intranasal administration of oxytocin have shown that this neuropeptide stimulates sensitive parenting and positive social behaviors.[12] Although work continues to determine the extent to which oxytocin affects our behavior in bonding, it can be said with certainty that this hormone is essential to our social structure.

Studies conducted on maternal physiology and behavior demonstrated that oxytocin, present in increased amounts during pregnancy, also strengthens the maternal–fetal attachment. During parturition, the levels of oxytocin in the brain increase due to vaginal and cervical stimulation, as the oxytocinergic system is activated. The oxytocin levels also notably increase in the maternal cerebral spinal fluid at parturition. For the child, although the human fetal brain is capable of producing oxytocin, because this neuropeptide can cross the placenta, it has been proposed that the mother produces much of the oxytocin the child experiences at parturition, as occurs in mammalian subjects.[13] As a study by Ruth Feldman et al. concluded, oxytocin measured during each trimester has consistent levels across pregnancy, while the oxytocin levels can predict postpartum maternal behavior and bonding and have a relation to mental and behavioral attachment.[14] Thus, it can be concluded that as current evidence suggests, maternal–fetal physiological communication through the neuropeptide oxytocin promotes the maternal–fetal bond.

Psychological Aspects of Maternal–Fetal Attachment

The maternal–fetal attachment developed during pregnancy is further enhanced by psychophysiological factors, as it is now better understood that a mother's emotional state affects fetal development, particularly prenatal stress. In mammalian subjects, prenatal stress has been shown to contribute to immune, endocrine, and neurobehavioral outcomes in the child. Likewise, maternal stress can alter the distribution and levels of neurotransmitters, and the responsivity of the hypothalamic-pituitary-adrenal axis, which has an essential role in fetal programming. For human mothers, studies assessed maternal psychosocial constructs, maternal behaviors, and sociodemographic characteristics to determine how psychophysiological communication occurs. Observations confirmed that maternal psychosocial processes independently affect gestation length and fetal growth. When analyzing further effects of prenatal

[12] Fabienne Naber et al., "Intranasal Oxytocin Increases Fathers' Observed Responsiveness during Play with Their Children: A Double-Blind Within-Subject Experiment," *Psychoneuroendocrinology* 35.10 (November 2010): 1583–1586.

[13] Ibone Olza-Fernández et al., "Neuroendocrinology of Childbirth and Mother-Child Attachment: The Basis of an Etiopathogenic Model of Perinatal Neurobiological Disorders," *Frontiers in Neuroendocrinology* 35.4 (October 2014): 459–472.

[14] Ruth Feldman et al., "Evidence for a Neuroendocrinological Foundation of Human Affiliation: Plasma Oxytocin Levels across Pregnancy and the Postpartum Period Predict Mother–Infant Bonding," *Psychological Science (Wiley-Blackwell)* 18.11 (November 2007): 965–970.

stress and social support on pituitary-adrenal hormones, results demonstrated that maternal stress increased concentrations of maternal ACTH (adrenocorticotropic hormone) and cortisol, while social support decreased these hormonal levels.

A continued effect of the higher concentrations on these stress-related maternal pituitary-adrenal hormones is linked to increased production of the placental neuropeptide CRH (corticotropin-releasing hormone). In primate pregnancy, CRH has a rich expression in the placenta and serves to regulate maternal–fetal pituitary-adrenal function, fetal cellular growth, differentiation, maturation, and the physiology of parturition.[15] Additional studies revealed that increased concentrations of maternal CRH predicted earlier onset of labor and preterm labor, and were associated with an increase in risk for fetal growth and maturation restriction.

The effects of prenatal maternal stress and stress hormones were observed to influence the child even for years after parturition, affecting infant behavioral reactivity and temperament, and thus demonstrating the significant breadth and duration of the maternal–fetal communication.[16] Furthermore, a pregnant woman who displays greater psychophysiological response to events or circumstances in her daily environment provides greater experiential conditioning of the fetal nervous system with positive consequences for development.[17]

A very compelling example of this concept in the maternal–fetal relationship is the story of the Visitation in the New Testament: "When Elizabeth heard Mary's greeting, the baby leaped in her womb" (Luke 1:41). Overjoyed with the arrival and visit of her cousin Mary, Elizabeth transferred her overwhelming sentiments to her unborn son, who upon hearing the jubilant voice of his aunt and experiencing the happiness of his mother leaped in his mother's womb.

A Remarkable Case

In a remarkable case of maternal–fetal relationship, a mother was diagnosed with Adrenal Insufficiency (AI) after being transferred to a university hospital, following rapid decompensation into cardiogenic shock, multi-organ failure, and becoming a candidate for heart transplantation. She was six months postpartum when she presented to the local hospital, after having had a successful and uneventful first pregnancy and vaginal delivery to a healthy baby boy. She had multiple visits to the emergency department for nausea and vomiting, weakness, fatigue, and a forty pound weight loss over the six months after the birth of her son. Initially unresponsive to treatments, she was finally diagnosed with AI.

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[15] Pathik D. Wadhwa, "Psychoneuroendocrine Processes in Human Pregnancy Influence Fetal Development and Health," *Psychoneuroendocrinology* 30.8 (September 2005): 724–743.

[16] Pathik D. Wadhwa et al., "Behavioral Perinatology: Biobehavioral Processes in Human Fetal Development," *Regulatory Peptides* 108.2–3 (October 15, 2002): 149–157.

[17] Janet A. DiPietro, "Psychological and Psychophysiological Considerations Regarding the Maternal–Fetal Relationship," *Infant and Child Development* 19.1 (January/February 2010): 27–38.

AI is a condition in which the adrenal glands do not produce adequate amounts of the steroid hormones cortisol and aldosterone. The incidence of AI in pregnancy is one in three thousand births. Unrecognized AI during pregnancy is associated with high incidence of serious maternal and fetal complications. For a mother with AI during pregnancy, serum cortisol levels will not be elevated as normally occurs, but will be at the concentrations of a non-pregnant woman.[18] After birth, the serum cortisol drops to a dangerous level, leading to cardiogenic shock. Proper treatments with glucocorticoid and fludrocortisone in a timely manner prevent death. But the interesting and mysterious question remains as to how the mother survives the entire length of gestation and parturition.

Although still in question, AI is tolerated during pregnancy as the fetal steroid production supports and protects the mother. The fetal placental unit, composed of the placenta, fetal adrenal glands, and liver, is an interactive endocrine entity. Over 60 percent of the fetal cortisol is passed to the mother, making up approximately 6.6 percent of the total maternal cortisol. Therefore, as the maternal cortisol levels decreased due to AI, the fetal production increased, protecting the mother from the effects of severe AI until birth.[19] This case illustrates an extraordinary instance of maternal–fetal relationship wherein both supported and protected each other.

Fetal Imaging and Maternal–Fetal Attachment

The introduction of real-time ultrasound to the practice of obstetrics in the late 1970s has made a great contribution to the topic of maternal–fetal attachment. Before the invention of this technology, a pregnant woman's first realization of life inside her womb was at the "quickening" (first fetal movement) stage of gestation. Women viewing the early fetus by means of ultrasound imaging expressed emotions and thoughts clearly affirming a bond of loyalty toward the fetus.[20] The presentation of fetal images via ultrasound early in pregnancy before any bodily cues are experienced has superseded the earlier importance of quickening for the mother's realization of actual life inside the womb and may contribute towards stronger feelings of attachment to the unborn child and enhanced health behavior during pregnancy.[21]

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[18] See Mahdi Kamoun et al., "Adrenal Disease during Pregnancy: Pathophysiology, Diagnosis and Management Strategies," *American Journal of the Medical Sciences* 347.1(January 2014): 64–73; Gareth Seaward et al., "Addisonian Crisis in Pregnancy. Case Report," *British Journal of Obstetrics and Gynecology* 96.11 (November 1989): 1348–1350; and Daesman Suri et al., "Assessment of Adrenal Reserve in Pregnancy: Defining the Normal Response to the Adrenocorticotropin Stimulation Test," *Journal of Clinical Endocrinology and Metabolism* 91.10 (October 2006): 3866–3872.

[19] William E. Rainey et al., "Fetal and Maternal Adrenals in Human Pregnancy," *Obstetric Gynecology Clinic North America* 31.4 (December 2004): 817–835.

[20] John Fletcher et al., "Maternal Bonding in Early Fetal Ultrasound Evaluations," *New England Journal of Medicine* 308.7 (February 17, 1983): 392–393.

[21] B. Sedgmen et al., "The Impact of Two-Dimensional versus Three-Dimensional Ultrasound Exposure on Maternal–Fetal Attachment and Maternal Health Behavior in Pregnancy," *Ultrasound Obstetric Gynecology* 27.3 (March 2006): 245–251.

Elective Cesarean Section, In Vitro Fertilization, and Surrogacy

An examination of the effects of artificial reproductive techniques and elective cesarean sections must also be considered in light of the maternal–fetal attachment. As has already been seen, maternal–fetal communication is a complex interaction that establishes the earliest bond in a human being's life, evident from conception to parturition. Therefore, any artificial means of reproduction or elective parturition may have severe and long-lasting effects on the health of the child, and also on the formation of early bonds.

In vitro fertilization (IVF), the process of manually combining an egg and sperm in a laboratory dish and then transferring the embryo to the uterus, removes the effects of the maternal preparation for the fetus which occurs in the presence of the gametes in natural conception. As the environment for implantation and the implantation itself occur artificially, it is unknown whether the lack of the early physiological effects may detrimentally affect pregnancy, development, and attachment for the mother and child. Studies conducted to compare mothers who conceived naturally versus those who conceived via IVF revealed that IVF mothers experienced significantly higher anxiety levels and depression.[22]

In cases of surrogacy, an artificial reproductive technique in which a surrogate mother is implanted with the embryo in place of the biological mother, introduces a reproductive act completely void of the physiological and psychophysiological maternal–fetal communication that is essential to the bond between the mother and child. In this case, the formation of maternal–fetal attachment is not possible and instead occurs between a surrogate mother who may have no further interaction with the child beyond parturition, despite the vital bond formed during pregnancy.

Furthermore, even in instances of natural pregnancy, elective cesarean sections, in which the mother chooses to have a cesarean section over a natural delivery without medical reason, have been proven to have detrimental consequences for the child. A cesarean section disrupts the endocrine mechanisms of the maternal–fetal attachment, particularly as the many physiological effects of labor are eliminated. The surge of vasopressin and noradrenaline is lost, and decreased levels of cortisol and catecholamines are evident, which have been related to increased cases of respiratory distress after elective cesarean sections.

The mother also demonstrates lower levels of hormones and neuroendocrinological factors after a cesarean section, which may affect the maternal–fetal attachment, particularly as neuroimaging studies have shown that mothers have significantly reduced responses in the brain to their child's cries as compared to mothers who had vaginal births.[23] In each instance, the maternal–fetal attachment is disrupted,

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[22] Catherine Ann McMahon et al., "Anxiety during Pregnancy and Fetal Attachment after In-Vitro Fertilization Conception," *Human Reproduction* 12.1 (February 1997): 176–182.

[23] Ibone Olza-Fernández et al., "Neuroendocrinology of Childbirth and Mother–Child attachment: The Basis of an Etiopathogenic Model of Perinatal Neurobiological Disorders," *Frontiers in Neuroendocrinology* 35.4 (October 2014): 459–472.

although the immediate and far-reaching effects of this absence of maternal–fetal communication is not fully understood. Considering the vital and intricate nature of maternal–fetal attachment to a human being, and the detrimental effects artificial means of reproduction and birth have on the child and mother, medical and scientific endeavors would be of better use in improving the care and assistance for natural means of conception and parturition.

The Earliest Relationship

There is no doubt that the earliest relationship between a mother and a child does not begin with birth. At the very core of the human society stands the bond formed between a mother and child, which is developed from the earliest stages of pregnancy through maternal–fetal physiological and psychophysiological communications. Not only would a better understanding of the intricate workings of this communication serve to better our functioning as a society, as our world seeks to improve our interactions and friendships, it may also shape the path to take in care, respect, and dignity for the maternal–fetal attachment as a whole.

Apart from the care provided until parturition, this may also lead to informed and conscientious choices regarding conception and birth. A recent study was conducted to test for correlations between maternal–fetal attachment and health practices. The health practices included factors that affected mother and child health during pregnancy, such drug and alcohol use, diet, exercise, and prenatal care. It was determined that a significant correlation existed between lower maternal–fetal attachment and fewer positive health practices.[24] Therefore, by improving maternal–fetal attachment, overall prenatal health may improve.

In addition, with an increase in artificial means of conception and birth, such as IVF, surrogacy, and voluntary cesarean section, our society and each individual health care provider and expecting family must consider what consequences to the development of the fetus and the formation of the attachment between a fetus and mother may occur. Although these become increasingly sought-out solutions for assisted conception and childbirth, not enough is known about long-term detrimental effects—particularly as prenatal attachment has shown a correlation with later attachment, having possible life-long effects.

While much research has been conducted on maternal–infant attachment, not as much has been completed for maternal–fetal attachment.[25] Taking both current research and the need for further research in this area into account, it would be of immeasurable benefit to the child, the mother, and each society of every nation to seek as complete an understanding as is possible of this intricate and beautiful maternal–fetal bond: the first friendship developed at the beginning of human life.

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[24] Kelly Lindgren, "Relationships among Maternal–Fetal Attachment, Prenatal Depression, and Health Practices in Pregnancy," *Research in Nursing and Health* 24.3 (June 2001): 203–217.

[25] Jeanne L. Alhusen, "A Literature Update on Maternal–Fetal Attachment," *Journal of Obstetric, Gynecologic, and Neonatal Nursing* 37.3 (May/June 2008): 315–328.