

On the Psychodynamics of Preeclampsia and HELLP Syndrome: Recent Advances in Treatment

Rupert Linder

Abstract: In medical science it is well known that the uterine conditions during the time of implantation are crucial. The “mother embryo crosstalk,” or the communication between embryo and mother, lays the foundation for the later health of both, on a basic biological and psychological level. A new and unique synopsis of current knowledge about implantation with psychological findings of patients affected by preeclampsia or HELLP (hypertension, elevated liver enzymes, and low platelets) syndrome shows striking interrelations. For the first time a psycho-dynamic understanding of these life-threatening conditions comes into reach. This gives rise to new prevention and treatment modalities.

Keywords: Mother embryo crosstalk, Preeclampsia, HELLP Syndrome

Preeclampsia and the HELLP Syndrome are important clinical conditions because they are of great significance in health policies and the health of mothers of babies. For decades, a close link with conditions in early stages of pregnancy (i.e. bad placentation hypothesis) has been suspected by medical science as causal. The aim of this paper is to clarify the psychological relationships related to these conditions.

There are three parts:

1. Knowledge about the manifold physiological processes during early pregnancy;
2. Findings from bodily therapeutic courses about mental processes during exactly this period; and
3. Examples that give an impression of the early imprinting from this period in the lives of adults with appropriate case histories.

Knowledge of Early Pregnancy

In scientific literature, the medical conditions preeclampsia and the more severe forms of eclampsia and HELLP Syndrome are combined under the generic term pregnancy induced hypertension (PIH). Preeclampsia is characterized by increased blood pressure of the pregnant woman, proteinuria and the formation of oedema. The HELLP Syndrome gets its name from H: hypertension, EL: elevated liver enzymes and LP: low platelets. Despite its being life threatening (bleeding disorder, liver failure), it is often only expressed clinically only by light upper stomach pains. The diagnosis is made by means of characteristic blood values. The significance for health policies is very high: worldwide over 50,000 women die of PIH every year. In industrial countries it occurs in 2 – 5% of pregnancies and is the second highest cause of maternal mortality in 12 – 18%. It is responsible for 25% of perinatal mortality in children. When occurring up to the 24th week of pregnancy it is responsible for 65% of maternal complications and 82% of child mortality (Rath & Fischer, 2009).

Is it possible that such a serious illness can be related to psychological factors? I well remember a discussion with my esteemed colleague Susanne Bässler in a gynaecological working group in Karlsruhe in the mid-1990s. She replied at the time to my psychosomatic speculations, “That is impossible because medical science has just established that PIH is related to early placentation. It therefore can’t be caused psychologically.” On the other hand, medical science has increasingly accepted that early imprinting of people in many aspects (fetal programming) through the circumstances of the children before birth (Gluckman, Hanson, Cooper, & Thornburg, 2008; Nathanielsz,

2006; Van den Bergh, 2011). Fetal programming states that the roots of physical illness may be in the prenatal period, and has increasingly included psychological attitudes and behaviours (Räikkönen, Seckl, Personen, Simons, & Van den Bertg, 2011; Van den Bergh, 2005; 2011).

Burkard Schauf (2008), previously senior physician of obstetrics at the University Gynaecological Clinic in Tübingen, now chief physician of the Gynaecological Clinic of the Sozialstiftung Bamberg, gave an unforgettable lecture on the topic, "Fetal programming, diabetes, hypertension, preeclampsia: What influence does the uterine environment have on later life?" Schauf's noticeable empathy with the unborn child was remarkable. This was also expressed in his body language. During this early time of life (implantation and early placental development), he described the early dialogue of the child's cells with the mother's immune cells, "Hallo [Hello] T-helper cells, let us spread ourselves in the endometrium and keep the killer cells at bay." This is then a good basis for successful placentation.

As a matter of fact, implantation is prepared and modified by different influences: hormones, immune cells, and peptides. The endometrium is prepared and thickened by the hormone estradiol during the woman's monthly cycle. It can reach a thickness of 7 – 14 mm as observed via ultrasound, whereby the doubled thickness, namely the front and back, are measured and appear with a delicate light centre line. The actual endometrium is relatively dark due to its high water content. At ovulation the cells around the burst follicle change and the resulting corpus luteum produces the progesterone that alters the secretion of the uterus and prepares ideal conditions for the implantation of the embryo. When the embryo has migrated into the uterus and contact is made with the endometrium around the fifth day after conception, some of the embryonic cells produce the human chorionic gonadotropin (HCG) that stimulates the corpus luteum to further activity, and the production of progesterone. The highest value is reached by about the 11th week of pregnancy, after which the placenta becomes increasingly capable of producing progesterone itself.

This is scientifically spoken of as "mother-embryo crosstalk" (the communication between mother and embryo). A Google internet search for this keyword results in 135,000 hits. Fujiwara (2006) differentiates a "systemic crosstalk," in which the substances or cells transmitted by blood convey messages and a "local crosstalk," which occurs directly at the implantation site. Very complex processes play a role here. For instance, in the middle of the luteal phase the cells of the corpus luteum produce a particularly large number of receptors for chorionic gonadotropin, which the embryo produces in precisely this phase. The HCG is a characteristic of humans and primates. There is also an equine specific form, but other species of mammals have other mediators (prolactins, interferons). The HCG alone is not sufficient, however, there are additional mechanisms of combined crosstalk. Fujiwara discovered that *in situ* early contact develops between the embryonic cells and local immune cells at the implantation site. The human PBMCs (Peripheral Blood Mononuclear Cells) pick up the information that an embryo is present and, after migration, transmit this through the blood to many other tissues. This has a positive effect on the pregnancy as seen by the corpus luteum in the ovary. Therefore, the effect together with the HCG is much greater than that with HCG alone. The fact that other substances soluble in blood plasma can perform this function in humans was excluded by Kratzer and Taylor (1990).

Early immunological and other contacts are described by Fujiwara (2005), as well as by Fazelli & Pewsey (2008). These contacts are important for all developmental stages from the gamete maturation to late pregnancy. They differentiate different signals. Messengers for long distances (long-range signals or LRS), such as progesterone, immobilize the musculature of the fallopian tube and reduce the movement rate of the cilia in the tube. They also affect growth hormones, growth factors, and various lectins. Messengers for short distances (short-range signals, or SRS) do not yet display as uniform a picture as do LRS. At least it could be recently demonstrated (Georgiou et al., 2007) that the presence of an egg cell or sperm cells in the fallopian tube in organ culture *in vivo* changed the nature of the protein secretion of the tube, and in different ways depending on if and which gamete/s are present. These could even be divided into four different active categories: protein production and repair, antioxidants,

metabolism, and miscellaneous. Spermatozoa have influence on prostaglandin metabolism and thus apparently facilitate their migration to the fertilization site. Sperm cells are able to bond with local fibrinogen and thus are better protected against phagocytosis. The appropriate regulation of proteins for the egg cells is important, such as Alpha-2-HS-glycoprotein, which prevents the spontaneous hardening of the zona pellucida, a problem that occasionally arises in *in vitro* fertilization. The conclusion is that the interaction between gametes, embryo, and the female genital tract (FGT) form a complex interactive network which leads to the creation and preservation of the pregnancy. The dysfunction of this network leads to the dysfunction of fertility, miscarriage, or even the impairment of the state of health of offspring in adulthood.

On the one hand, the immune defense in the FGT is essentially important for resisting pathogens. One only has to think of the open wound present at menstruation and after birth. As we know, the vagina is not a germ-free zone. There is a multitude of different microorganisms that are held in check at the threshold of the inner genital tract and the cervix. On the other hand, we have been previously able to learn that the immune system performs an important messenger function in early pregnancy. In this sense certain "inflammatory responses" are even a prerequisite for pregnancy.

A local inflammatory response in the endometrium (in this case caused by a previous endometrium biopsy) may increase the rate of implantation (Dekel, Gnainsky, Granot, & Mor, 2010). Koga and Mor (2010) described "toll-like receptors" (TLR) that perform important functions at the contact site between mother and child. They play a large role in the regulation of normal and pathological processes. Additionally, through immune cells recruited at the implantation site, high levels of pro-inflammatory T-helper cells (Th-1) and cytokines (IL-6, IL-8, and TNF α) develop that are characteristic of the period of early implantation.

Macrophages are important messengers. They present in large numbers during the entire pregnancy at the boundary point between mother and embryo. They are recruited from decidua and trophoblast cells (Renaud & Graham, 2008). But uterine dendritic cells (uDC) are indispensable for the pregnancy (Pollard, 2008; Plaks et al., 2008). A macrophage colony stimulating factor-1 (CSF-1), which activates the formation and increase of monocytes and dendritic cells in all mammals, is established in the maternal decidua. The dendritic cells, which have a kind of morphological similarity with nerve cells because of their many appendages at the front and only one at the rear, are the antigen presenters for the other immune cells. Macrophages are important in deciding which antigens are tolerable and which have to be combated. On the other hand they also have their own trophic functions, and they are necessary, in combination with the hormones estradiol and progesterone, to facilitate an effective decidual transformation of stromal cells into epitheloid cells at the implantation site. The decidual cells grow by means of rapid proliferation in an arc around the embryo. After complete implantation the embryo is totally surrounded by a primary decidual zone of polyploid cells and a secondary decidual zone of diploid cells.

A further important growth-promoting function is the facilitation of vascularisation, i.e. the formation and development of the vasculature supply. Capillaries grow from the uterine artery into the decidua. In this way vessels are created with a large dilated lumen with maternal blood that bathes the decidual villi. As described by Plaks et al. (2008), the uDCs partially regulate this vascularization by means of their synthesis of TGF-Beta1 and sFfl-1 (soluble fms-like tyrosine kinase-1, s. also below). Implantation is not possible by elimination of the uDC in an animal model. These are therefore essential for a successful pregnancy.

In a detailed summary, Furuya, Ishida, Aoki, & Fukamizu (2008) wrote about the pathophysiology of placental disorders in pregnancy-induced hypertension. Different life-threatening illnesses during pregnancy, such as pregnancy-induced hypertension, are closely related to a dysfunction of the placenta. Cumulative studies suggest that a hypoxic microenvironment at the site of implantation, the pure stress, the uterine placental blood flow, and pro-inflammatory substances erroneously secreted

into the maternal vascular system all contribute synergistically to the progression of PIH. So, for example, the soluble form of the receptor for the vascular endothelial growth factor (receptor-1, sVEGFR-1) and the soluble form of endoglin (CD105) are elevated in the circulating blood of PIH mothers. In the review, current knowledge about placenta development and the pathophysiology of the placenta in hypertension pregnancy disorders is exhaustively described. In addition, the latest results of vasoactive messengers in PIH and PIH rodent models are discussed. A variety of angiogenetic molecules and proteolytic enzymes play a decisive role in the bringing about of placentation and the development of the placental circulatory system.

Adamson et al. (2002) describe two different ways in which the trophoblast cells penetrate into the uterus. First, in the very early post-implantation period, the trophoblast cells can infiltrate through the activation of the trophoblast giant cell-specific gene *Plf* that regulates the production of proliferin and stimulates invasion closely associated with the spiral arterial system. Second, beginning from day 12.5 after fertilization (p.c.), the cell can penetrate in a more diffuse variation interstitially, going into the decidua basalis that is not regulated by *Plf* but by the spongioblast-specific gene *Tppb*. The development of the placental vascular network between days 10 and 17 p.c. is impressively represented three dimensionally in this study by a plastic cast.

The vascular endothelial growth factor (VEGF), the fibroblast growth factor (FGF), and the placenta growth factor (PlGF) are indispensable during the entire pregnancy (Reynolds & Redmer, 2001); in addition a proliferation-promoting and additional angiogenetic function of the above mentioned HCGs plays a role here (Zygmunt, Herr, Münstedt, Lang, & Liang, 2003).

In the later phases, trophoblast villi and on the fetal side vessels of terminal villi form a finely differentiated vascular network. The fetal weight almost doubles in the last trimester of pregnancy. On the other hand, the weight of the placenta hardly increases in this period. Instead the network of vessels in the terminal villi/the labyrinth becomes better differentiated and the functional capacity of the capillaries on the fetal side and of the maternal blood sinuses also increases (Furuya et al., 2008). In contrast to invasion by cancer cells, which is in some ways similar to the vascularization processes at the implantation of the embryo, the trophoblast invasion is finely regulated and controlled by the local pro-inflammatory microenvironment. This applies with respect to the immunological tolerance and the well-regulated development of the vasculature supply. By intrauterine growth retardation (IUGR), however, the differentiation of the terminal villi is often disturbed and the thickening of the distal villi becomes evident (Kraus, Sobin, & Tocker, 2004).

The placenta's arterial circulation has no autonomous innervation and is therefore regulated by local signals such as pressure and blood flow (Myatt, 1992). If the implantation process does not occur well enough the placenta suffers from inadequate perfusion and secretes various types of pro-inflammatory molecules which, as a result, damage the maternal endothelial cells (EC) and increase vessel. This also damages the maternal organs and impairs the fetal placental environment.

The increase in the antiangiogen-effective sFlt-1 in proportion to the angiogen-effective PlGF (placental growth factor) and VEGF (vascular endothelial growth factor) plays a substantial role in the development of preeclampsia and growth retardation. The proportion can be determined from the blood and is currently being developed as an additional diagnostic test (Akolekar, Syngelaki, Poon, Wright, & Nicolaides, 2013; Rana et al., 2012; Tallarek, Huppertz, & Stepan, 2012). There are already studies that show that prolongation of the pregnancy can be achieved through an extracorporeal apheresis (extraction of proteins from the blood) of the sFlt-1 in preeclamptic pregnancies (Thadani et al., 2011).

In addition to these direct vasoactive mechanisms, the activation of the renin-angiotensin system (RAS) has recently been focused on in the pathogenesis of the conditions of preeclampsia and HELLP Syndrome.

Additionally, autoimmune reactions also come into play as autoimmune antibodies against the angiotensin II receptor type 1 (AT 1) have been found in the serum of preeclamptic women (Dechend et al., 2006; Wallukat et al., 1999). The relationships and clinical significance of these antibodies, the RAS and immune reactions are presently the subject of several investigations (Freitag et al., 2013; LaMarca et al. 2011; Parrish et al. 2011; Stepan et al., 2006).

As there are very few possibilities of examination of pregnant women the diagnosis of placental circulation depends primarily on Doppler sonography examination, more precisely ultrasound biometry, cardiotocographic examinations (CTGs) and the histological examination of the placental tissue after birth.

Findings from Body Therapy

I am grateful to the team from the Institute for Pre- and Perinatal Education (IPPE) for the following information, particularly Karlton Terry, Kathryn Kier, and Max Peschek. In courses they deal with the personal exploration of early phases of human development and the healing of wounds from this period. I am also grateful that I was able to take part in one of these courses. For the aspects that are discussed here, two periods of human development play a significant role: Implantation, the period in which the embryo adheres to the uterine mucin layer and grows into it and Discovery, the point in time when the mother discovers that she is pregnant.

According to teachings at IPPE, the early embryo migrates through the fallopian tube, “falls” into the lumen and “chooses” a place in the lumen, or rather on the uterine mucin layer which is at this point greatly built up. It is then able to select a certain point by rolling. Finally it attaches itself to a point on the uterine mucin layer (apposition) and adheres more tightly to the mucin layer (adhesion). Then connections grow, shoots from the embryo growing into the maternal mucin layer. Figure 1 shows schematically that different conditions are waiting here: the heart represents love and joyful expectation, the chef’s hat represents appetizing provisions; however, the dark stain represents all the mother’s wounds, perhaps a previously lost child, suppressed and side-lined emotions, the schnapps glass represents alcohol or other harmful substances.

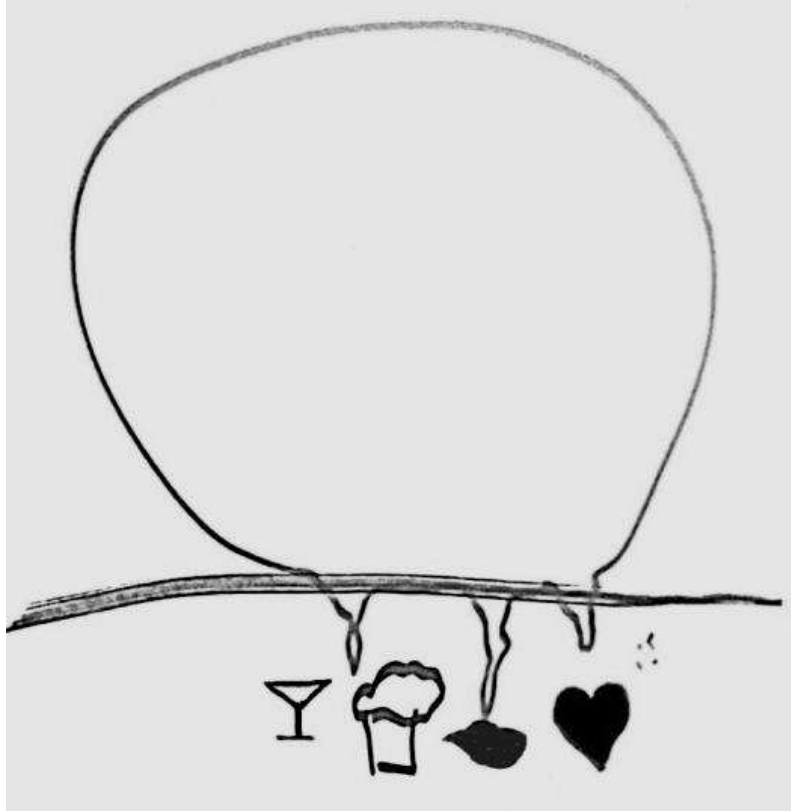


Fig. 1 Course material IPPE; see text for explanation

The conditions for the child can be very different: luxurious, satisfying, pleasantly warm, or bare, arid, or cool. The child can implant itself but gives up all its desires. About 40 % of the children are able to implant themselves successfully in the uterine mucin layer, the other 60% not. (Diedrich, Fauser, Devroey, & Griesinger, 2007)

How realistic these connections look is shown in the following illustration of the implantation site from Gray's Anatomy (1918):

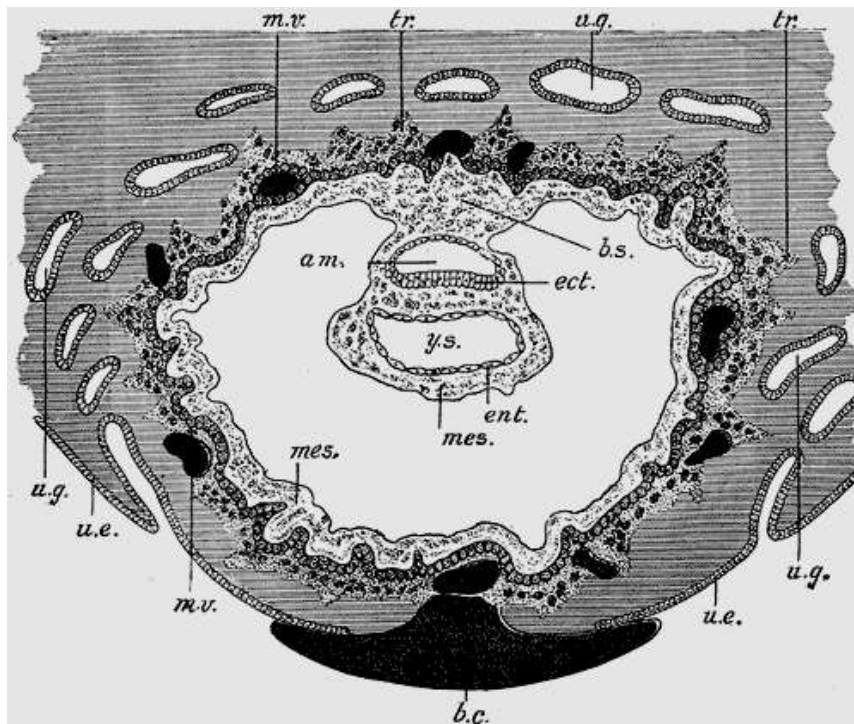


Fig. 2 Section through ovum imbedded in the uterine decidua (Gray 1918)

Caption: **am.** amniotic sac; **b.c.** blood clot; **ect.** embryonic ectoderm; **ent.** endoderm; **m.v.** maternal vessels; **mes.** mesoderm, **tr.** trophoblast villi, **u.g.** uterine glands; **y.s.** yolk sac

After implantation, the mother discovers that she is pregnant. This produces continual emotional disturbance (löst regelmäßig einen inneren Gefühlssturm bei ihr aus) because her own internal feelings have also been activated. This moment is often shortly after the non-appearance of her period. Sometimes it is earlier (due to the very sensitive tests for HCG, some women sense internal transformations immediately after conception). There is a rating of conceivable reactions of the mother to the child, listed here from spurning to the welcoming:

1. Unsuccessfully attempts abortion
2. Goes for an abortion but has second thoughts at the last minute
3. Child unwanted, disaster, thinks about "doing something to get rid of it"
4. Child unwanted, disaster, thinks about abortion
5. Child unwanted, negative thoughts, "maybe it'll work"
6. Child unwanted, but accepted
7. Child wanted, but not now
8. Child wanted, but should be of a specific sex
9. Child wanted, but for a reason that has nothing to do with the child
10. Child fully welcomed to be itself, relaxed

Two further circumstances could also be significant: namely, that children can be wanted too much (over wanted) or that the pregnancy is celebrated too much, both of which tend towards point 9, the child is wanted for a reason other than itself.

These early emotional constellations are of extreme importance for the relationship between these two people (mother and child). For the mother, this is the first opportunity for awareness of the child to come into play. At this time during pregnancy, every level of emotion resonates. These are often unconscious to the mother herself because they originate from her early and earliest existence, such as feelings from her own period of implantation and discovery, or even from unconscious (epigenetic) imprinting of her own forebears and family history.

These run like a “golden thread” through all of the child’s life - sometimes spoken, often only implied, often silent. In my practice I often meet with these questions when caring for pregnant women who are confronted in a new way with their own emotions during their new pregnancy. They are often aware of the facts from previous generations, but the psychological significance and the internal relationships are not yet emotionally obvious to them.

The development of this understanding is frequently associated with the sensation of considerable pain that is mourning previously missed emotional and concrete possibilities between these two people. The presence of people who are not easily shocked by these issues but can provide secure support is very helpful in this process. This can be done, for example, by means of art therapy (Evertz, 2008), body therapy (Emerson, 2014; Peschek, 2014; Terry, 2014), bonding analysis (Raffaj, 2014; Schroth, 2014), or by means of psychotherapeutic-oriented support during pregnancy (Linder 2010).

During pregnancy, these feelings are particularly strong and thus offer the chance of being better understood psychologically and cognitively. Sometimes great disappointment towards one’s own mother and/or father can be felt. In the long run, it is important to understand that the behaviour of the parents that was difficult to bear didn’t generally arise from their own conscious decision but that they themselves were similarly victims driven by their own family system. As a rule the more unconsciously this occurred, the stronger the effect is on the descendants. Consistent with this is the fact that women who were themselves unborn children in unwanted pregnancies often get into the situation of having an unwanted pregnancy. (Linder, 2008a; 2008b).

The processing of such biographical backgrounds provides chances of relieving the children from such burdens. This is a comfort for the pregnant women who are often very concerned. They might say something like, “Well, if I’m feeling so terrible, how does that affect my child? I ought to be in the best possible condition. And now I keep on crying.” In reality these are tears of relief when suitable support and security are provided. And the comfort and gain is that the adults can set aside a part of their biographical burden and the children will be freed from the burdens of the past. This task is emotionally hard work, but for these reasons definitely worthwhile.

In this context, the words of the English pediatrician and psychoanalyst, Donald W. Winnicott, who spoke of the ordinarily “good enough mother” are notable. He extended the trauma of birth as described by Rank (1924) to the entire period before birth and considered this to be formative of the whole person. The expression “umbilical affect” for this phenomenon was introduced into psychoanalytical terminology by the English psychoanalyst Francis Mott (Terry, 2011). One of his basic convictions was, “Every psychological feeling derives from an older physical feeling.”

An extremely important topic in the umbilical period is, “how can we get what we need?” It is obvious that this is a question from the umbilical period, but it remains significant for every stage of life. We need:

- Food,
- Money,
- Love,
- Intimacy,
- Self-respect

All these items are important requirements which already play a role in the implantation and discovery periods. But, as is evident, they have an indispensable lifelong function for every person.

Therefore different strategies are developed and practiced early on, such as worming oneself in, cheating, stealing, bargaining, begging, or sacrificing oneself

It is clear that not every one of these possibilities is particularly successful life-long or socially acceptable. One purpose in life (and especially the work of psychotherapy) is to refine strategies that had possibly been of help in earlier periods, and also to acquire new ones. It is possible to be free to find out which possibilities are best suited to the prevailing situation in life.

The umbilical affects correspond precisely to the period and the process of placentation. They represent the emotional side of the processes that have long been regarded by medical science as decisive in setting the course of the early relationship between mother and child. The roots of the problems which can later lead to preeclampsia or HELLP Syndrome can be found here.

Of course, men are also affected by emotional historical experiences. This was the case when these men were unborn children in the early phases of development and failed to receive nurturing from their fathers. Expectant fathers who are confronted with their own early emotional past can come to terms with paternity and accompany their pregnant wives. Strong negative emotional reactions to the woman's pregnancy often have their own biographical background in this area.

Case Histories

The following case histories depict experiences and life histories that have to do with preeclampsia or HELLP Syndrome. Ms. A. (Case History 1) suffered from preeclampsia and a premature birth with her own daughter, and her mother suffered from it with her older sister. She was strongly ambivalent toward her mother and her marriage. In the case of Ms. B. (Case History 2) her mother was badly affected by preeclampsia. The situation and previous history was described from her mother's point of view. Here, it becomes immediately clear how life threatening the grandmother's living situation was in her own prenatal period. Ms. C. (Case History 3) was affected as a child by her mother's preeclampsia at the end of her pregnancy with her. Here again a deep-reaching insecurity can be felt, which was more or less passed on from the mother to the daughter. Ms. D. (Case History 4) had HELLP Syndrome twice. Again her own deep insecurity is reflected in relation to her mother as well as in the relationship with her own oldest child. The intensive psychotherapeutic support during the second pregnancy could not, admittedly, prevent the renewed occurrence of a HELLP Syndrome, however it did in an impressive way make possible much more understanding and a sensitive relationship with the second child.

Case History 1

Thirty-eight-year-old Ms. A. came to my gynaecological psychotherapeutic practice. Her question was: "I want clarification with respect to further family planning for a second child or not. Four years ago I had severe eclampsia and my daughter was born prematurely by caesarian delivery in the 29th week of pregnancy." The birth weight was 850 g (below the 10th weight percentile), the Apgar score was 3 / 4 / 6 (after 1, 5 and 10 minutes). From the hospital records the medical emergency was evident: rising blood pressure despite attempted intravenous therapy using magnesium and Nepresol. The doppler examination showed the child's circulation to be already centralized, the cardiotocograph (CTG) was limited. The patient was already displaying neurological abnormalities, the liver values were rising and the thrombocyte values were falling.

"All the doctors advise me against a new pregnancy. It's very deep-seated. It's a very big issue for me. My daughter is developing well so far."

Ms. A is a highly qualified professional in the field of early learning. "I'm also suffering from constantly recurring doubts about my marriage. Fantasies about separation have almost always been

there, except during our first months together when I was very much in love. Other men sometimes fascinate me.”

Ms. A is the middle child of three children. The birth of her older sister (+ 18 months) was very confrontational and dramatic as an emergency caesarean delivery had to be carried out due to preeclampsia. “I came into existence ‘by accident’.” In addition, the mother had reckoned with having a boy and was absolutely convinced that she would. She herself was then delivered “completely without conflict” two weeks before the expected date by planned caesarean section. This was described by Ms. A’s mother as the most pleasant birth of all. She was not breast fed. The mother also described difficulties with bottle feeding. She fed very slowly and sometimes she unexpectedly spit up everything up again, especially when her older sister screamed.

“My mother described me as difficult. I experienced little real inner or physical closeness. Her own mother and the older sister were always interfering and overbearing and she couldn’t stand up to it. My mother felt that my father wasn’t ‘up to bringing children up,’ so that she kept us mainly away from him and undertook the task of upbringing.” He was then considered to be too authoritarian by the family and was not respected. In the course of therapy the early relationship situation was also discussed many times. For example, in the form of a dream: *she and several others were on a walk and came to a sort of filling station kiosk. They all wanted something to eat. The sales assistant said she had nothing to eat, she wouldn’t want anything. She made it very clear that she didn’t really want to sell us anything. However, on the counter in front of her there was food such as was in a bakery. She said she only had warm bread and butter. Everyone was delighted with that, as they all wanted something warm. The sales assistant had not reckoned with that.* Here, eating and food are symbols relating to implantation, and so this dream could be seen as an example of “cross-talk” or when the early embryo is negotiating food supply and connection with the mother’s surrounding (uterine wall and lining).

At one point, the early life situation of Ms. A’s mother was talked about. She had been born during the war. Prior to this there had been a furious quarrel between her parents. The father had volunteered out of conviction to serve as a soldier. She herself had been conceived during his home leave. Soon after, the father was reported missing in the Russian campaign and was later declared dead.

Here it is easy to understand how the mother’s own earlier life situation had been reactivated by her pregnancies. After all, she herself had been conceived in a difficult relationship situation of the parents, had had to do without her father from early on, and her mother had doubtlessly found it very hard to cope with this loss.

Ms A.’s mother therefore was very anxious during the pregnancy with the sister as well as with her and still felt very insecure after her birth. Even during therapy Ms A. could still feel her mother’s anxiety when on the phone with her. She described how difficult it was for her as an adult to let her mother hug her and how close she came to tears then.

She also related how she herself, had felt unsure and never really comfortable during her pregnancy with her daughter.

Time and again she describes her earlier life situation. It was, as described above, typical of and analogous to the early implantation phase by preeclampsia, “I know that my parents wanted to practice contraception, but I still came into being. I also came too early and moreover was the “wrong” sex. I have never experienced being properly welcomed. I can never feel really at ease. Even inside me I can’t really say yes. Inside me I’m running away. I always, even in a group, have the feeling of not belonging. I don’t like to be noticed, speak quietly and experience a feeling of oppression.”

The early implantation and discovery periods came up again and again. Not only cognitively but above all from the viewpoint of emotional feelings. In some partner dialogues the relationship ambivalences were cautiously addressed. The internal doubts were expressed repeatedly. It was important for her to be able to understand that these doubts about herself and the relationship were a

part of her and could be explained on the grounds of her previous history. So she was able to experience the internal relationship to herself increasingly as “special” but ongoing. “They are just a part of me...”

After 25 sessions (spread over 3 years) therapy could be concluded. The question of having a child remained unresolved. The relationship with her husband however had succeeded in becoming much more trusting. She was able to venture gradually on a closer and more affectionate relationship with her husband. Holiday situations were much more relaxed than previously. She was able to tolerate her daughter becoming more independent. She could allow her husband to take responsibility as a partner in parenting. Professionally, she was able to involve herself successfully in the furthering of her career.

Case History 2

The next case history is special because it describes the situation of preeclampsia from the grandmother’s point of view.

In my practice I happened to hear that the daughter of a patient that I’ll call Ms B., suffered from very severe preeclampsia during pregnancy. She is the younger of 2 sisters. While on holiday a doctor had to be called because of stomach pains in the 32nd week of pregnancy. She was already delirious (seeing evil faces, confusedness). Emergency transport by helicopter to a specialist hospital was undertaken and preparations were already made for immediate delivery and emergency caesarean. The expectant father was told that it would be a miracle if he were to see his wife and child alive. Amazingly the child (a son), although only 1,000 grams, was comparatively healthy and did not even require intubation. The mother had to remain in intensive care for eight days with total kidney failure. Not until the fifth day did urinary excretion begin again. Extubation was completed two days later. Mother and son (and father, too) later made a complete recovery.

About the grandmother’s previous history, in the second half of the 1930s, Ms B.’s mother had a boyfriend who was studying and from a “good” family. Ms. B.’s mother even supported him financially while he was studying. She became unintendedly pregnant. In her desperation she went to her gynaecologist, Dr Kuppenheim, in Pforzheim (see below). He encouraged her, saying, “*You’ll manage it. You’ll have pleasure in your child in the future.*” She decided to keep the child, who turned out to be the very same Ms. B. It wasn’t possible, however, to get married. Her parents demanded that she move to another town and have the child there because of the “disgrace.” So she lived with an aunt in a neighboring city. Ms. B. was prematurely born at seven months gestation weighing 2,250 grams. She found the time spent with the aunt very enjoyable; the mother was very affectionate to her. She carried her in her arms for two years. “I still have this feeling of being cared for inside me.” She never got to know her father. The child maintenance was, however, always paid punctually. Ms. B. married and had two children. Her marriage, however, broke up after some years. She is extremely socially involved. The other daughter suffered for many years from depressive moods and had an unhappy first marriage. In the meantime, there has been a considerable improvement in her psychological state and a happy second marriage.

As can be seen from this case history, the issue of eclampsia moves along a fine line between love, life, and death. In this story the gynaecologist also plays a special part. He himself had a special life history that was characterized by charitable work, commitment to life, and in the end mortal danger. I believe at this point he should be remembered for playing a large role in the history of our town and being representative of our country. Therefore, his story will be briefly outlined here:

Rudolf Kuppenheim MD was born in 1865 in Pforzheim, studied medicine in Heidelberg and was the first gynaecologist to practice in Pforzheim. In 1893 he became chief physician of the Obstetric Clinic of the Protestant Siloah Hospital in Pforzheim. In the First World War he received the title of medical consultant on account of his great services and various decorations due to his commitment and valor. His two sons also served, partly voluntarily, in the First World War and received prestigious awards.

After his conversion from Judaism to Protestantism he was also an elder of the church. On 1st April 1933 he and 7 other doctors in Pforzheim had their medical licenses revoked on the grounds of their Jewish descent. At this point he was also forced to resign from the hospital. He was able to continue his private practice until September, 1938. The meeting with Ms. B.'s mother had taken place the year before.

The persecution and harassment kept on getting worse. On 21st October 1940, the 50th anniversary of the day that the spouses Rudolf and his wife, Lily met, Sturmabteilung (SA) men told them both to be ready to leave in an hour. They committed joint suicide and were found dying in their home, a cushion with the decorations won in the First World War on a table. The sons Hans and Felix managed to escape abroad.

Case History 3

Ms. C., 45 years old, began psychotherapy because of strong fears of being abandoned when there were disagreements in her marriage. "I have an exaggerated need for harmony." She has suffered a great deal under this need, because it has been with her for many decades now. She describes her mother as "somewhat reserved", but always correct and never loud. There had never been a real mother/daughter feeling. Ms. C. describes her father as temperamental, affectionate, "no matter what problem I had, he resolved it for me or with me."

He was a war exile and had to move to where the mother lived. The parents had got to know each other at the age of 15 in a dance course. The mother's parents had wanted to prevent the liaison by all means, as being a refugee he was not of the same social class. The mother was beaten and she was sent to a job in a more northern city over 200 km away. The father then rode for six hours there on his moped every weekend and visited her. Ms. C. had great difficulties in detaching herself from her parents during adolescence. She had severe depression and some suicide attempts. She ended up finally in inpatient psychotherapy in another town.

As additional previous history, it must be noted that towards the end of the pregnancy with Ms C. the mother developed preeclampsia with elevated blood pressure and severe fluid retention. She was born 4 weeks prematurely and the birth took place under a short-duration anesthetic. She came directly after being discharged from hospital to her mother's mother, who also brought her up for a long time. The mother had often had to suffer very much under the severity and harshness of her own mother, and been able to develop very little self-esteem. Ms. C. worked initially at the reception of a charitable institution. Although dependable and friendly she sometimes found it difficult when planning schedules to muster sufficient determination to reconcile differing interests.

Sometime after having had a baby, she went a bit strange: She imagined that she was erotically attracted to women. She told her friends this as a sort of coming-out. Today she says that it was more of a notion than otherwise. Her husband then moved out of the home. When it seemed that he was going to start new relationship she successfully did all she could to win him back. In the meantime Ms C. has successfully weathered the adolescent conflicts of her children. During the ongoing therapy she has been able to increase her own self security considerably. As a human being she has managed to attain considerably more access to her inner authenticity and strength, which for some time had already been her professional assets in a successful career.

Here the deep insecurity in being and in the early relationship is perceptible. This can be explained by the profound insecurity already present in the mother, probably from her own early trauma. This was certainly aggravated if not reactivated by the short-duration anesthetic during delivery. The mental states and the circumstances of her earliest period of life (implantation, discovery, birth) and their underlying factors were gone over repeatedly; in this way the emotional aspects were cautiously perceived and moderated in their impact on the present time, and a biographical sorting process and

substantial break-through was made possible. So she was able to rediscover a deep emotional attachment and communication at first with her father, but afterwards also with her mother.

Case Study 4

Ms. D, a 30-year-old woman, was being cared for during her second pregnancy. She had a neat and smart appearance but was reserved in utterance. The emotional vibrancy in her speech and body language was reduced, her basic demeanor seemed apprehensive.

At the end of her last pregnancy in the 38th week, the year before, Ms. D. had been admitted to the gynaecological department of a neighboring hospital due to rising liver values and undetermined back problems after personal consultation with the senior physician. There, a day later, she had caesarean section on account of further rising liver values and incipient HELLP Syndrome. The child, a boy, (3,080 g) had a good Apgar score (9/10/10) but was transferred to a paediatric clinic two days later after two convulsive seizures. "Our little boy had strange symptoms. Since yesterday he's twitched (minimally) for several minutes in the daytime, now he's in the intensive care unit of the paediatric clinic with a lumbar puncture, antibiotic therapy, and is getting anti-convulsants." Several days later she came to the practice with her husband who seemed supportive and loving.

The child's transfer to the (distant) pediatric clinic had certainly affected her. At this point she was offered psychotherapeutic support to help her and her child come to terms with the stress and the events described. At the time she didn't take advantage of the offer. At the follow up examination, she could partially breastfeed, the boy didn't cry as much, everything was within normal parameters. At some other appointments she continually talked of "a funny twitching and tingling" in her hands and feet. For this reason she had consulted various doctors over the last six months. A neurologist, found by her mother, had examined her thoroughly and had also found "nothing really wrong." An MRI scan and other examinations had been carried out. She had the feeling that she had a serious illness. She had also thought about possibly suffering from multiple sclerosis, in the meantime she would be happy at least to know what she did have. At the age of 5 months her son had had a MRI scan due to suspected renal pelvis dilation which was not confirmed. He was doing really well, he was starting to crawl and everything was developing age appropriately.

One month later she is again pregnant, in the seventh week. She still has the strange tingling as well as a peculiar pain in her leg. The neurologist is of the opinion that an antidepressant could help and speaks of a depression affecting the body. Ms D. now also agrees to preventive psychotherapy.

She came from a former German colony in Eastern Europe. At the time of her conception, her parents were living with the mother's parents/foster parents in a small flat but, "they got on well with each other." After her birth the father was allowed to move to Germany, but her mother and herself not until three years later. She only saw her father twice during this period. She had a good relationship with her mother. She had been a "mummy's girl," very shy and lovingly cared for. The mother was not good at bringing discussions to a close, but withdrew at some stage. The father had managed to establish himself in industry in Germany and had worked his way up and qualified as a master. Even though he was understanding, he was also strict, particularly when she couldn't do well enough in math. There had always been disagreements, and quite often quarrels, between the parents because of the father's views about money, child upbringing, and other things. He had just been an authoritarian man. The parents' religious belief (protestant free church), which had been the basis of everyday life, was a support for them all.

Her mother had been given to foster parents before she started school. She had however "already known" her birth parents. There is no longer any contact with a two year younger brother. Ms D. can provide no other information on this point.

Additionally, in regard to the course of her pregnancy, her husband was taking two months parental leave. A few times she missed appointments, especially when she was supposed to bring information about the history of her family. She complained of sleepless nights caused by her son's teething problems. He cried every quarter of an hour and she had to give him a painkiller. The tingling problems, however, were getting less and the other complaints were practically gone. Nevertheless she held her breath when saying this and she perceptibly lost contact to her base. "I'd rather have depression with crying fits." During the last pregnancy she had felt pretty well, there'd only been the funny back pains. This was also the case at the last appointment before her referral to hospital. Then there suddenly came the time where something had to be done. "In the end we were powerless. Maybe I did hold back much of how I really felt." Whether it made sense to give her antidepressants during the pregnancy? – I argued for restraint in this respect. She said, "I find my case somewhat odd." Various complaints of her son continually played a role as well as (indirectly) the resulting demands or restrictions in her life. The back pains were successfully treated by gentle orthopaedic means. She lived in a flat above her parents-in-law. Only sometimes things were said carefully, which suggested criticism of the relationship with her mother. She got on better with her mother-in-law than with her mother. Her mother liked helping, also many other people, but never really listened properly.

She continually talked about her son's complaints and sickness. In so doing, discussion of her own suffering and her state of mind took a back seat. Visits to the doctors and the medication were talked about. Her own uncertainty, even reticence, was evident. On one occasion her son cried audibly in the waiting room below without her visibly reacting to it (32nd week of pregnancy). She continued to suffer sleep disturbances on account of her son. But she also had her own ailments. She had a circulatory disorder and the feeling of not being able to breathe properly. In a CTG, a three minute long continuous contraction of the uterus attracted notice. Regular measuring of the blood values was started. Elevated liver values were again evident. These were regularly checked. She had to continually clear her throat because of a little dry cough. Her state of mind and her results were patiently monitored. The child's growth was good. In the 33rd week of pregnancy the child's size was calculated in an ultrasound examination to be a week further on, with an estimated weight of 2,248 g. In the 36th week weight was estimated at 3,415 g, in the 38th week 3,589 g. She still had a series of slight complaints; itchiness of the arms and shoulders and restless legs, which improved on walking around. No matter how she lay nothing was right. Sometimes her bed was too warm and then it was too cold. On examination the uterus was sometimes found to be relatively hard and sensitive. Once she was occupied by the question: how does the purification of the amniotic fluid work, how is the urea removed?

Ms. D's mother had doubtlessly been despondent after the births of two of her younger siblings. But it was difficult for Ms. D. to speak with her about it. The liver values continued to rise and thrombocyte values to fall. I consulted colleagues. I exchanged views with a friend who is a senior physician (Dr. Deutsch, Karlsruhe) who agreed that it was a chronic subclinical HELLP Syndrome, which could remain stable for some time. It was important for the thrombocyte value not to fall below 100,000. Some time later I consulted with Prof. Schauf of the University Clinic in Tübingen who advised inducing the birth, especially as it was already at the beginning of the 39th week of pregnancy. A holiday was approaching. I asked the midwife if it were possible to do a blood test but she refused on the grounds of this being too great a responsibility in this case. After being examined in the clinic where first a contraction stress test with oxytocin was carried out and it was normal, Ms D. asked for a day to think it over. The next day she tried inducing the birth. The cervix did not dilate further so another caesarean section was carried out under epidural anaesthetic. The child was delivered at 9 pm in the evening of the holiday in very good condition: 3,490 g, an Apgar score of 9/10/10, an umbilical artery pH of 7.34. On the day after, when I phoned the postnatal unit, the nurse in the unit said immediately "Oh, is that the woman who is looking after the child so touchingly? She's already mobile on the 2nd day. The lowest thrombocyte value was 108,000. She says herself that she's fine, everything is ok, and she's feeling

much better than the last time.” A very long time was taken trying to achieve a normal birth. The child was very easy to look after, sleeps in the evenings, was breastfed twice each night, then went on sleeping.

He continued to develop well. This time, Ms. D. was quite sure that she would be able to breastfeed properly and fully and managed to do so. The first time she hadn't managed it. This is really quite astonishing considering how often she had felt unwell during pregnancy. All the to-ing and fro-ing before the birth had been pretty difficult but the delay before the second induction had been very important for her. The older son was also doing relatively well. He was affectionate towards his brother. Occasionally he also had infections but fewer problems than before the birth. After three months she was worried that she might become depressed again. She had the tingling in her feet only occasionally.

Once again the subject of the previous biography of her mother came up. Her mother had had a good relationship with her foster parents. (Once again her dry little cough was to be heard.) She said that her mother's mother had died from an embolism when her mother was 3-months old. There was also an older brother. The father took a new wife. The new wife then said, “There are too many children here. One of them has to go.” The mother was almost put into a children's home, which had a dreadful reputation in this country. Then the dead mother's brother came and took her in. The current interaction between Ms. D and her mother was really strange. She would ask how things were but didn't really want to hear the answer.

In this session Ms. D. was able for the first time to begin to grasp how badly wounded her mother had been by her life history. In the following sessions she was able to remember that her mother had apparently suffered from postpartum depression after the birth of her younger siblings. With regard to her children, she noticed how intensely her younger son had always looked at her from early on. Also, how he had smiled at three months. He had also much stronger muscles than the older son, who had always looked past her when breastfeeding.

In the final session she again describes how the family history, in this case her mother's family, could have so great an impact. She could now better understand the interconnections. Up to then they had been like holes, waiting to be discovered. Her mother wasn't aware of these holes, but she couldn't ask her about them. A great, hard to bear tension is tangible in the countertransference which is probably related to the mother's life-threatening situation in her earlier lifetime.

Postscript: The deeper dynamics and background of the (grand)mother's wounds could only be worked out in the months after the second birth. One aspect deserves closer description: Preceding the second birth there were extremely fierce disagreements. Strange differences suddenly arose between the carers, who normally associated with each other in a trusting and friendly fashion. The hospital doctors couldn't understand why the practicing doctor had kept a woman with such pathological blood values in outpatient treatment for so long. The midwife, also a cooperative colleague for decades, was indignant about the impertinence of being asked to carry out a blood test. The practicing gynaecologist “didn't understand the world anymore” and wondered if they were all going crazy. Mutual anxieties were specified. The strong inner dynamic which had obviously transferred itself to the carers could be understood as the transfer of the inner conflict of the woman and the family history. It was, therefore, obviously important that the progress of the second birth greatly eased the undisturbed building of the relationship between Ms. D and her younger child. Such transfer phenomena have up to now not often been perceived in somatic medicine. It is, however, evident in this case how they can appear in the severe illnesses preeclampsia or HELLP Syndrome and how the perception, comprehension, and toleration of these phenomena are important for the deeper understanding of the dynamics of illness and the healing care of those affected.

A further case study can be found in the story of Peter in the chapter *Wie Kleinkinder Prä- und Perinatale Erfahrungen, chapter in der Psychotherapie zum Ausdruck bringen (How Children Express Pre- And Perinatal Experiences In Psychotherapy)* by the children's psychotherapist Antonia Stulz-Koller

(2014), in which the mother at once realizes in the first conversation “that something between her and the child was wrong from the start.” The very empathetically written case history describes a similar disruption of the relationship from the very start and its partial dissolution.

Summary

All of these case histories, which are enmeshed in various ways in the issue of preeclampsia or HELLP Syndrome, impressively portray the very deep emotional insecurity of the people affected. During therapy the overcoming of this insecurity is clearly observable in some cases.

This account of the issue is intended to give very different perspectives on the background factors to preeclampsia and HELLP Syndrome. The range is wide - from scientific knowledge about the earliest stages of life to the manifold interactions between mother and child, from the depiction of the realms of experience of the implantation and discovery periods in current body therapeutic self-experience and precise description of psychological phenomena from those most closely affected. In the process the parallelism of the early phases of pregnancy and severe illness in later phases of life stands out. They all suffered from specific ramifications in the pivotal realms of relationships. This was obviously the issue in both illnesses that runs through all three levels. The lifelong fundamental question is, “How is life in a relationship possible?” In case history 4 a second generation trauma is being dealt with, because the origin lies in the severe traumatization of the grandmother. She was apparently so unconsciously trapped in shock that the pregnant daughter remained so shocked in the areas of her motherliness that she could not enable the implantation and vascularization processes to take place “adequately enough.” Of particular note, the processes observed in case history 4 appeared of the fissuring situation transferred to the therapeutic teams, which in itself could be an important development for mother and child. That this could even be revealed was only due to the trusting relationship between the somatic carers that had grown over many years. The inter-disciplinary working group was able to address this issue with precision and empathy.

References

- Adamson, S.L., Lu, Y., Whiteley, K.J., Holmyard, D., Hemberger, M., Pfarrer, C., & Cross, J.C. (2002). Interactions between trophoblast cells and the maternal and fetal circulation in the mouse placenta. *Journal of Developmental Biology*, 250(2), 358-373.
- Akolekar, R., Syngelaki, A., Poon, L., Wright, D., & Nicolaides, K.H. (2013). Competing Risks Model in Early Screening for Preeclampsia by Biophysical and Biochemical Markers. *Fetal Diagnosis and Therapy*, 33, 8–15.
- Dechend, R., Homuth, V., Wallukat, G., Müller, D.N., Krause, M., Dudenhausen, J. ... & Luft, F.C. (2006). Agonistic antibodies directed at the angiotensin II, AT1 receptor in preeclampsia. *Journal of the Society for Gynecologic Investigation*, 13(2), 79-86.
- Diedrich, K., Fauser, B.C.J.M, Devroey, P., & Griesinger, G. (2007). The role of the endometrium and embryo in human implantation. *Human Reproduction Update Volume 13(4)*, 365-377.
- Dekel, N., Gnainsky, Y., Granot, I., & Mor, G. (2010). Inflammation and Implantation. *American Journal of Reproduction Immunology*, 63(1), 17-21. doi: 10.1111/j.1600-0897.2009.00792.x.
- Emerson, W. (2014). Prä- und perinataler schock: ein universelles leiden [Pre and perinatal shock: A universal suffering], in *Lehrbuch der Pränatalen Psychologie [Textbook of prenatal psychology]*, Evertz, K., Janus, L., & Linder, R. (Eds.), Heibelberg: Mattes Verlag.
- Evertz, K., (2008). A Visual Exploration of the psychodynamics in problematic pregnancies: Case studies in analytic-asthetic art therapy. *Int. J. Prenatal and Perinatal Psychology and Medicine*, 20(3,4), 179 – 200.

- Fazeli, A., & Pewsey, E. (2008). Maternal communication with gametes and embryos: A complex interaction. *Briefings in Functional Genomics*, 7(2), 111-118.
- Freitag, N., Tirado-González, I., Barrientos, G., Herse, F., Thijssen, V.L, Weedon-Fekjær, S.M., ... & Blois, S.M. (2013). Interfering with Gal-1-mediated angiogenesis contributes to the pathogenesis of preeclampsia. *Proceedings of the National Academy of Sciences of the United States of America*, 110(28), 11451-11456.
- Fujiwara, H., (2006). Immune cells contribute to systemic cross-talk between the embryo and mother during early pregnancy in cooperation with the endocrine system. *Reproductive Medicine and Biology*, 5, 19-29.
- Furuya, M., Ishida, J., Aoki, I., & Fukamizu, A., (2008). Pathophysiology of placentation abnormalities in pregnancy-induced hypertension. *Vascular Health and Risk Management*, 4(6), 1301-1313.
- Georgiou, A.S., Snijders, A.P, Sostaric, E., Aflatoonian, R., Vazquez, J.L., Vazquez, J.M., ..., & Fazeli, A., (2007). Modulation of the oviductal environment by gametes. *Journal of Proteome Research*, 6(12), 4656-4666.
- Gluckman, P.D., Hanson, M.A., Cooper, C., & Thornburg, K.L. (2008). Effect of in utero and early-life conditions on adult health and disease. *The New England Journal of Medicine*, 359(1), 61-73.
- Gray, H. (1918). *Anatomy of the human body*. Philadelphia: Lea & Febiger.
<http://en.wikipedia.org/wiki/File:Gray32.png>.
- Kratzer, P.G., & Taylor, R.N., (1990). Corpus luteum function in early pregnancies is primarily determined by the rate of change of human chorionic gonadotropin levels. *American Journal of Obstetrics & Gynecology*, 163(5, Pt 1), 1497-1502.
- Koga, K., & Mor, G., (2010). Toll-like Receptors at the Maternal-Fetal Interface in Normal Pregnancy and Pregnancy Disorders. *American Journal of Reproductive Immunology*, 63(6) 587-600.
- Kraus, F.T., Sobin, L.H., & Tocker, J.T., (2004). Anatomy, structure and function. In Kraus, F.T., Redline, R.W., & Gersel, D.J. (Eds) *Placental Pathology*. Washington DC: American Registry of Pathology, 1-22.
- La Marca, B., Wallace, K., Herse, F., Wallukat, G., Martin, J.N., Weimer, A., & Dechend, R., (2011). Hypertension in response to placental ischemia during pregnancy: Role of B lymphocytes. *Hypertension*, 57, 865-871.
- Linder, R. (ed.) (2008a). *Liebe, Schwangerschaft, Konflikt, und Lösung – Erkundungen zur Psychodynamik des Schwangerschaftskonflikts [Love, pregnancy, conflict, and resolution - explorations to the psychodynamics of pregnancy conflict*. Heidelberg: Mattes Verlag.
- Linder, R., (2008b). Conflict of Pregnancy – Experiences from a gynaecological and psychotherapeutical practice, *Int. J. Prenatal and Perinatal Psychology and Medicine*, 20(1/2), 4-11.
- Linder, R., (2010). Overcoming somatic and psychological difficulties: New experiences from an integrated linkage of obstetrics and psychotherapy. *Journal of Prenatal and Perinatal Psychology and Health* 24(4), 201-209.
- Myatt, L., (1992). Control of vascular resistance in the human placenta. *Placenta*, 13(4), 329-341.
- Nathanielsz, P.W., (2006). Animal models that elucidate basic principles of the developmental origins of adult diseases, *The ILAR Journal*, 47(1), 73-82.
- Parrish, M.R., Wallace, K., Tam Tam, K.B., Herse, F., Weimer, A., Wenzel, K., ... & LaMarca, B., (2011). Hypertension in response to AT1-AA: Role of reactive oxygen species in pregnancy-induced hypertension. *American Journal of Hypertension*, 24(7), 835-840.
- Peschek, M., (2014). Psychologische Aspekte des ersten Schwangerschaftsdrittels [Psychological aspects of the first trimester of pregnancy] in *Lehrbuch der pränatalen psychologie [Textbook of prenatal psychology]*, Evertz, K., Janus, L., & Linder, R. (Eds.). Heidelberg: Mattes Verlag.

- Plaks, V., Birnberg, T., Berkutzki, T., Sela, S., Yashar, A.B., Kalchenko, V., ... & Jung, S., (2008). Uterine DCs are crucial for decidua formation during embryo implantation in mice. *The Journal of Clinical Investigation*, *118*, 3954-3965.
- Pollard, J.W. (2008). Uterine DCs are essential for pregnancy. *The Journal of Clinical Investigation*, *118*, 3832-3835.
- Raffaj, J., (2014). Die Niederschläge des Abhängigkeitskonflikts der Eltern im intrauterinen Raum [The precipitation of the dependency conflict of parents in the intrauterine space] in *Lehrbuch der Pränatalen Psychologie [Textbook of Prenatal Psychology]*, Evertz, K., Janus, L., & Linder, R. (Eds.). Heidelberg: Mattes Verlag.
- Räikkönen, K, Seckl, J.R., Pesonen, A.K., Simons, A., & Van den Bergh, B.R.H. (2011). Stress, glucocorticoids and liquorice in human pregnancy: Programmers of the offspring brain. *Stress*, *14*(6), 590-603.
- Rana, S., Powe, C.E., Salahuddin, S., Verlohren, S., Perschel, F.H., Levine, R.J., & ..., & Karumanchi, S.A. (2012). Angiogenic Factors and the Risk of Adverse Outcomes in Women with Suspected Preeclampsia. *Circulation*, *125*(7), 911-919.
- Rath, U., & Fischer, T. (2009). Diagnostik und Therapie hypertensiver Schwangerschaftserkrankungen [Hypertensive disorders of pregnancy diagnosis and treatment]. *Deutsches Ärzteblatt International*, *106*(45), 733-738. Also in English: <http://www.aerzteblatt.de/int/archive/article?id=66607&src=search>
- Renaud, S.J., & Graham, C.H. (2008). The role of macrophages in utero-placental interactions during normal and pathological pregnancy. *Immunological Investigations*, *37*(5), 535-64.
- Reynolds, L.P., & Redmer, D.A. (2008). Angiogenesis in the Placenta. *Biology of Reproduction*, *64*, 1033-1040.
- Schauf, B., (2008). Fetale programmierung – diabetes, hypertonus, präeklampsie: Welchen einfluss hat das intrauterine milieu auf das spätere leben [Fetal programming - diabetes, hypertension, pre-eclampsia: The influence of the intrauterine environment on later life. Vortrag auf dem XVIII. Internationalen Kongress der ISPPM Prävention – Früher Dialog [Paper presented at the XVIII International Congress of ISPPM Prevention - Early dialogue]. Heidelberg.
- Schroth, G., (2014). Die bindungsanalyse nach J. Raffai [The bonding analysis by J. Raffai], in *Lehrbuch der Pränatalen Psychologie [Textbook of Prenatal Psychology]*, Evertz, K., Janus, L., & Linder, R. (Eds.). Heidelberg: Mattes Verlag.
- Stepan, H., Faber, R., Wessel, G., Wallukat, G., Schultheiss, H.P., & Walther, T. (2006). Relation between Circulating Angiotensin II Type 1 Receptor Agonistic Autoantibodies and Soluble fms-Like Tyrosine Kinase 1 in the Pathogenesis of Preeclampsia. *The Journal of Clinical Endocrinology & Metabolism*, *91*, 2424-2427.
- Stulz-Koller, A., (2014). Wie Kleinkinder prä- und perinatale Erfahrungen in der Psychotherapie zum Ausdruck bringen [How children express pre- and perinatal experiences in psychotherapy]. Chapter in *Lehrbuch der Pränatalen Psychologie [Textbook of Prenatal Psychology]*, Evertz, K., Janus, L., & Linder, R. (Eds.). Heidelberg: Mattes Verlag.
- Tallarek, A.C., Huppertz, B., & Stepan. H., (2012). Präeklampsie, aktuelle diagnostik und klinisches management, neue therapieoptionen und zukunftsansichten [Preeclampsia – aetiology, current diagnostics and clinical management, new therapy options and future perspectives]. *Geburtshilfe und Frauenheilkunde [Obstetrics and Gynecology]*, *72*, 1107-1116.
- Terry, K. & Team (n.d.). Institute for Pre- and Perinatal Education. Umbilical Affect, Booklet <http://www.ippe.info/publications/booklets.html>
- Terry, K. (2014). Pre- and Perinatal Baby Therapy, in *Lehrbuch der Pränatalen Psychologie [Textbook of Prenatal Psychology]*, Evertz, K., Janus, L., & Linder, R. (Eds.). Heidelberg: Mattes Verlag.

- Thadhani, R., Kisner, T., Hagmann, H., Bossung, V., Nocack, S., Schaarschmidt, W., ..., & Benzing, T., (2011). Pilot study of extracorporeal removal of soluble fms-like tyrosine kinase 1 in preeclampsia. *Circulation*, *124*(8),940-950.
- Van den Bergh, B.R.H., Mulder, E.J.H., Mennes, M., & Glover, V. (2005). Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: A review. *Neuroscience & Biobehavioral Reviews*, *29*, 237-258.
- Van den Bergh, B.R.H., (2011). Developmental programming of early brain and behaviour development and mental health: A conceptual framework. *Developmental Medicine & Child Neurology*, *53* (Suppl 4), 19-23.
- Wallukat, G., Homuth, V., Fischer, T., Lindschau, C., Horstkamp, B., Jüpner, A., ..., & Luft, F.C. (1999). Patients with preeclampsia develop agonistic autoantibodies against the angiotensin At1 receptor. *The Journal of Clinical Investigation*, *103*, 945-942.
- Zygmunt, M., Herr, F., Münstedt, K., Lang, U., & Liang, O.D., Angiogenesis and vasculogenesis in pregnancy. *European Journal of Obstetrics & Gynecology and Reproductive Biology*, *110*(Suppl 1), S10-8.