

# **Watch out for destructive stress factors affecting the developing brain**

## **- Enlighten pregnant women as a preventive action**

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### **Introduction**

Glucocorticoids are stress hormones released into the bloodstream due to numerous factors that changes the normal condition in the body, for example high fat diet, restricted food intake, infection and mental illness. Likewise different types of inflammatory disorders, for example asthma and allergy, is treated with synthetic glucocorticoids. During pregnancy the maternal levels of cortisol, the main stress hormone in humans, is several times higher than the fetal bloodstream. The fetus is protected from the high levels of cortisol thanks to the placental enzyme 11 $\beta$ -hydroxysteroid dehydrogenase type 2 (11 $\beta$ -HSD2). The enzyme converts a large portion of maternal cortisol to inactive cortisone before it reach the fetal blood. The cortisol that is not converted inhibits the fetal synthesis of cortisol, which contributes to the protection. Due to lower efficiency of the 11 $\beta$ -HSD2 enzyme, excessive maternal stress response or, treatment with synthetic glucocorticoids will expose the fetus to toxic levels of cortisol. The consequences could be lower birth weight, shorter pregnancy and structural and physiological alterations in the fetal brain that in the long run, may affect the mental health of the child during youth and adult life.

### **Decrease the fetal exposure**

It's hard to totally avoid increased glucocorticoids levels during pregnancy as there are many stressors in the everyday life. However, it's important to inform of these potential stressors to prevent excessive cortisol levels. Increased dissemination of information to pregnant women would be an easy way to rise the understanding how to avoid some of the stressors, for example high fat diet. Despite research the last decades pregnant women are still treated with synthetic glucocorticoids during asthma, for instance budesonide and fluticasone, that cannot be converted by 11 $\beta$ -HSD2 in the placenta and will hereby get transferred to the fetus. However, there are several other asthma medicines that are more superior to use for the treatment during pregnancy, for example prednisone and prednisolone. Women should get better information when it comes to the different treatments, and the possible side-effects for the fetus but also, the negative consequences on the placenta due to oxidative stress because of untreated asthma. Also, more research should be directed to the alternative treatment with ABCB1 that could protect the fetal brain from exposure to dangerous and harmful levels of glucocorticoids. ABCB1 is naturally located in the brain in both adults and fetus but is minimally expressed until after birth. If this protein could be added to the fetal bloodstream during pregnancy, it may protect the fetal brain from negative alterations and may avoid later psychical illness. Psychical illness is not just a disability in everyday life for the individual itself, but also for relatives and is highly effecting the society. It may not only be grounded in the amount of cortisol the fetus is exposed to during pregnancy, but it can be of great importance when it comes to brain development.

### **Factors increasing maternal and fetal cortisol levels**

Nutrition factors during pregnancy is important for normal development of the fetus. High fat diet or restricted food intake have been detected as influencing factors to increased levels of

cortisol in the maternal- and fetal bloodstream. Both diets inhibit the efficiency of the enzyme  $11\beta$ -HSD2. Moreover, high fat may also cause oxidative stress and cell damage in the placenta. Excessive intake of liquorice or caffeine the enzyme gets inhibited which will contribute to fetal exposure to cortisol. Chorioamnionitis is a fairly usual infection in the membrane surrounding the fetus in the uterus, causing an inflammation, and is hence considered as a stressor for the mother and can cause increased levels of cortisol. Many women experience increased anxiety during pregnancy, and this is associated with an over activity of maternal stress response. Likewise women suffering of depression during pregnancy have higher risk of increased levels of cortisol, but are also more strongly affected by stressors than healthy women. Since treatment with synthetic steroids is essential in some cases, for example during asthma or allergy, it's hard to avoid increased levels of stress hormones in the maternal bloodstream. Therefore, it's important to use glucocorticoids with as little transfer capability through the placenta as possible as well as a good affinity to  $11\beta$ -HSD2 so that it can convert the glucocorticoid to inactive form.

### **Consequences on the fetal brain**

It has been verified that increased levels of cortisol in the fetal bloodstream causes degeneration and negative structural changes in several areas of the fetal brain. The neurons get an alteration in morphology and therefore the communication in the brain becomes difficult. The stressors also induce an over activity of microglia cells, a type of macrophage that eats other cells, and result in loss of mass in some regions of the brain. It exists several hypotheses linking prenatal stress and later mental illness of the child. For example, prenatal stress, in form of smoking and anxiety, is associated with ADHD and depressive symptoms in the child. Also severe maternal stress e.g. losing a close relative during pregnancy may increase the risk for the offspring to develop schizophrenia.

### **References**

Neijd M. 2015. Ökad halt av stresshormon under graviditeten kan orsaka negativa förändringar i avkommans hjärna. Självständigt arbete i biologi. Uppsala universitet.