

# To know the fetus, to see the fetus and to treat the fetus

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How a fetus spends its time in the mother's womb had always been a mystery until now. Hence, the concept of diagnosing and treating the illnesses that afflict fetuses is a rather recent development. However, despite numerous clinical trials in the attempt to find effective treatment for fetuses, we still have a lot of room left for improvement. This failure to achieve satisfactory results in the treatment of fetuses is due to our lack of physiologically and biochemically understanding of the fetus itself. Therefore, in order to diagnose and treat the diseases of the fetus, we need to improve our understanding of the fetus. Here, based on the consensus that we have today, I would like to present to you an alternative approach to this issue concerning fetal health by using the data in our institute.

1) Understanding the fetus through the analysis of the fetal heart rate variability.

There are numerous oscillatory phenomena associated with the fetal heart rate variability. Each and every change in the heart beat, influences from the mother and daily biorhythmic changes, environmental changes can all influence the fetus' heart rate variability. When we are looking at a fetus, we need to remember that the changes in the fetal heart rate and rhythm are influenced by multiple controlling factors. It has been proven that the fetal heart rate variability is controlled by the circadian rhythm and some other extrinsic factors. These influences not only come from the mother but also from the fetus' own genetic biological clock.

In order to analyze the mechanisms behind the fetal heart rate variability without being confounded by the extrinsic and genetic factor mentioned above, there is a need to change our approach and mindset. The fetal heart rate variability displays, what we described in Mathematics, a nesting or fractal property. This fractal property is not influenced by the circadian rhythm and therefore is stable. However, it has been shown when a human fetus experiences acidemia, this stable fractal dimension collapses. Using this unique property, we have acquired a tool to distinguish hypoxemia from acidemia. The ability to derive the fetal ECG through the mother's abdominal surface is important in the accurate analysis of the fetal heart rate variability. We have successfully developed a clinically viable method to obtain the fetal ECG.

2) Understanding the fetus through fetal brain damage.

Although fetal acidemia can be detected by analyzing fetal heart rate variability, it is still inconclusive whether fetal acidemia is the cause of damage to targeted organs. From the results of the PET scans of the brains of sheep fetuses, we found out that acidemia causes a dramatic decrease in glucose metabolism. One of the most

possible clinical outcomes of this phenomenon is PVL. Experiments using animal models have demonstrated that changes and decreases in blood pressure contribute to PVL. Infections during gestational period also increase the risk of developing PVL.

3) Understanding the fetus through the nutritional viewpoint.

Recently, developmental origins of adult health and diseases (DoHAD) are receiving more and more attention from both the scientific and clinical communities. Dietary and nutritional problems faced by the mother have been shown to adversely affect fetal development. It has been demonstrated that poor fetal nutrition contributes to a greater risk of intracranial hemorrhage in the event of hypoxemia. It was also reported that infections might trigger a series of events that lead towards developmental defects of oligodendrocytes, and thus behavioral problems in life later. In addition to these established findings, I would like to explain the developmental origins of adult health and diseases associated with the mechanisms involving growth factors.

4) As one of the treatment for fetuses, using the mouse IUGR model, we have demonstrated that providing the mother with vitamin and folic acid supplements could alleviate IUGR. This points out that apart from invasive treatment, we could develop more convenient treatment options by understanding the fetus more.