



The Prediction and Prevention of Preterm Birth and its Consequences: An Unmet Challenge to Perinatal Medicine, Science and Society:

The Declaration of Dubrovnik

Preterm birth is the defining challenge to obstetrics and neonatology at the beginning of the XXI century. The advances in care of preterm neonates in the last decades has improved survival dramatically in developed and in developing countries, so that the definition of viability has been reframed. Yet, survival of the extreme premature neonate has come with high risk of long term disability. Therefore besides improved survival, the quality of life of these vulnerable infants should be emphasized by careful and lifelong evaluation of their progress. A legitimate question is whether neonatal medicine has approached the limit of intact extra-uterine life.

The success of neonatal medicine in treating the consequences of preterm birth has not been matched by the prevention of spontaneous or indicated preterm birth. The essential problem has been an incomplete understanding of the mechanisms of disease responsible for spontaneous preterm labor with intact or ruptured membranes or maternal and fetal disorders which result in indicated preterm delivery (e.g. preeclampsia and intrauterine growth restriction).

The taxonomy of obstetrical disorders responsible for preterm birth is in an early phase in which pathology is recognized by symptoms and signs rather the underlying mechanism of disease leading to these clinical manifestations. The time has come to use the tools of “discovery science” to indentify such mechanisms, as well as to find early biomarkers of risk and interventions aimed the prevention of preterm birth. It is now clear that preterm birth is not caused by only one pathologic process - but many. The naïve view that a single test and single intervention will prevent all cases of preterm birth should be recognized as an obstacle to progress. While infection/inflammation, vascular pathology and other mechanisms of disease have been identified, others remain to de discovered. A unique feature of pregnancy is the co-existence of two hosts in intimate contact with different genomes and environments. Moreover, while cooperation of the hosts should be expected, the biological interests of fetus and mother may not always coincide. Environmental exposures may have different effects on a mature host than in a developing organism. Viviparity has created conditions which allow for the potential development of unique pathologic process absent when there is not a symbiotic relationship and there yet unrecognized in medicine.

The identification of known (in other disciplines) and unknown mechanisms of diseases responsible for preterm birth represent the major challenge of perinatal medicine. Our discipline must commit itself to the use of the tools of “discovery science” and computational biology to meet this urgent need. This needs to be followed by rigorous translational science and ethically designed clinical trials.

At the same time, advances in understanding gained to date and the knowledge of promising clinically simple strategies to identify the patient at risk (e.g. vaginal pH testing to identify dysbiosis) and specific interventions to prevent preterm birth, deserve systematic and urgent rigorous testing because of their promise to achieve a dramatic and rapid reduction in the rate of this adverse pregnancy outcome.

The importance of behavioral, social and economic issues predisposing to prematurity, need to be recognized and addressed. We advocate adequate support and protection for pregnant women as an integral health promoting activity to prevent preterm birth in all cultures. Pregnant women in developing countries should be protected from hard work, mistreatment and any kind of exploitation as the causes of prematurity. Governments should encourage multidisciplinary approach in delivering care to pregnant mother and the newborn including at least obstetrical and neonatal care. This approach should be aimed to reduce perinatal and maternal mortality by up to 50 percent in the next ten years. It is also desirable to reduce prematurity rate between 32 and 36 weeks of gestation in developing countries by 50 percent within the next ten years.

Governments, scientific societies, funding bodies and charitable organizations which fund clinical and basic research need to realize the importance for society of the consequences of preterm birth. We believe that the prevention of preterm birth is possible if perinatal medicine, science and society give the necessary priority to this most urgent problem of maternal, fetal and neonatal patients.