

## Pursuing a New Paradigm of Preterm Birth: The Central Role of the Cervix

During her Maternal Fetal Medicine fellowship at the University of Chicago, and later as an obstetrician at the Hospital of the University of Pennsylvania, Dr. Michal Elovitz, Associate Professor of Obstetrics and Gynecology and Director of the Maternal and Child Health Research Program at the University of Pennsylvania, looked on in dismay as the treatments given to women facing preterm birth resulted in bad side effects and did not really prevent preterm birth.

“We give women magnesium sulfate. This drug inhibits muscles from contracting but the drug targets all muscles not just the uterus,” says Dr. Elovitz. “It made breathing difficult, and often it didn’t work. Despite treatment, many women still have a preterm birth. Some women deliver so early that the infant cannot survive or if the baby survives it faces enormous challenges. As a physician and mother, it was heart breaking.”

Over time, new treatment modalities were tried, but most continued to be ineffective. Which is why today, in 2014, 13 million infants worldwide continue to be born prematurely.

### Looking Beyond Obstetrics

Frustrated with the lack of progress, four years ago Dr. Elovitz came to a realization. “Our thinking was too insular and we needed to look beyond obstetrics,” she says. Her quest for a transdisciplinary approach led her to engage leading researchers in other fields such as bioengineering, immunology, pharmacology, and microbiology.

This research theme will determine the pathways that govern cervical change (or cervical remodeling) which must happen for fetal delivery to occur at any gestational age.

She soon arrived at a profoundly new insight: rather than the pathways for preterm birth beginning in the uterus — the accepted clinical wisdom at the time — she believed that key pathways in preterm birth might actually begin in the cervix. One of the key people she met and who is now a co-investigator for Theme Two of the March of Dimes’ Prematurity Research Center at the University of Pennsylvania is Louis Soslowsky, Ph.D.,

Professor of Orthopedic Surgery and Bioengineering in the School of Engineering and Applied Sciences at Penn.

Drs. Elovitz and Soslowsky are working together to measure the biomechanics of the cervix and responses to increasing “load.” As pregnancy progresses,



Dr. Michal Elovitz, M.D.  
Associate Professor  
of Obstetrics and  
Gynecology and  
Director of the Maternal  
and Child Health  
Research Program at  
the University of  
Pennsylvania

Premature birth is one of the most intractable health challenges in modern medicine:

- One in nine babies in the United States is born prematurely each year
- Premature birth is the leading cause of newborn death in children from birth to age five
- Nearly half a million babies are affected annually
- Premature birth costs society at least \$26 billion a year, according to the Institute of Medicine
- 15 million children are born prematurely every year worldwide
- Premature birth often leads to a lifetime of significant health challenges

The consequences of preterm birth extend to the entire family in terms of healthcare costs and impaired quality of life for the parents and siblings.

The March of Dimes Prematurity Research Center at The University of Pennsylvania is a robust, integrated cross-institutional effort. Its goal is to develop fundamental new insights into the biology of human pregnancy and the disease mechanisms of preterm birth to decrease the rate of prematurity and its associated complications. The March of Dimes intends to invest \$75 million over five years to support the National Campaign to End Premature Birth.

To accomplish its goal, the March of Dimes Prematurity Research Center at the University of Pennsylvania has developed three interrelated theme areas, each bringing together renowned thinkers, researchers, physicians and top academics to focus on key aspects of the underlying causes of preterm birth.

*continued*

## Pursuing a New Paradigm of Preterm Birth: The Central Role of the Cervix

the dynamic cervix must continuously adjust to support the weight of the growing fetus. In a normal pregnancy, the cervix remodels its structure to some degree but remains closed until labor occurs at term. Biomechanical processes must be involved in this but little is known. Drs. Elovitz and Soslowsky are asking whether if something in the biomechanical process goes awry in women who have a preterm birth.

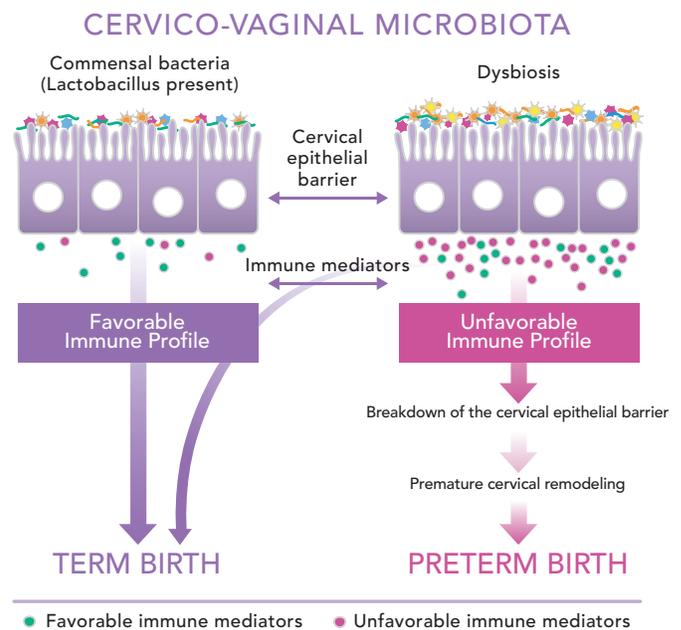
“Typically, for a tissue to change, genes and proteins would need to be altered. That process takes 4 to 24 hours,” says Dr. Elovitz. “What is so unique about the cervix is that it can change its structure in just minutes. The cervix remains rigid and closed for most of the nine months of pregnancy. When labor occurs, the cervix goes from a closed, fairly rigid structure to a thin, stretched out piece of tissue that allows the passage of a 7 lb (or more) baby. Then, in just minutes, it closes back up to prevent a woman from bleeding to death.”

While doctors know that this process occurs, they don’t know how it works and how these processes might be involved (or disrupted) in premature cervical remodeling. In Theme Two Dr. Elovitz’s team will also study biological events, such as inflammation, to understand how these factors alter how tissue responds to load.

### Seeking Answers

To answer these questions, the team aims to identify the processes that control cervical remodeling in preterm birth. One possibility they are exploring, for example, is that an altered microbiome in the cervix may accelerate cervical remodeling. The microbiome, is a community of bacteria that normally inhabit the body. Different body locations have different microbiomes. Early studies from Dr. Elovitz’s research show that the cervical vaginal microbiome may be different in women who go on to have a preterm birth.

“Our hypothesis is that there is shift in the microbiome or a dysbiotic state in the cervix and vagina that triggers preterm birth,” she says. “Whether caused by smoke or diet or other causes, a dysbiotic state develops that leads to an exaggerated immune response in the vagina and cervix. This immune response disrupts the epithelial barrier, which protects the cervix. Molecularly, it causes an influx of water into the tissue. The collagen fibers that are firm and tight, get dispersed and the cellular matrix breaks down.”



*A New Paradigm for Preterm Birth*

Dr. Elovitz is very hopeful. “I’m very excited by this work. With the March of Dimes funding, we will be able to further test our new hypothesis. If we are correct, then new therapies to prevent preterm birth become a realistic goal in our immediate future not decades away.”

For more information on how you can be a part of this effort, please contact

David “D.J.” Hampton II  
Senior Vice President & Chief Development Officer  
March of Dimes  
1275 Mamaroneck Avenue  
White Plains, NY 10605  
Phone: 914.997.4492  
[philanthropy@marchofdimes.org](mailto:philanthropy@marchofdimes.org)

You can make an online gift by clicking here:

**DONATE**

**march of dimes**  
prematurity research center  
The University of Pennsylvania

[www.prematurityresearch.org/penn/](http://www.prematurityresearch.org/penn/)