STEVE CARITIS ON WHAT'S BROKEN IN PRENATAL MEDICATION

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MARTHA RIAL

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As a child in the 1950s, Steve Caritis (Obstetrics and Gynecology Resident '73) loved taking apart appliances. When he dismantled the family toaster, his mother called him *mastro halasti*—Greek for "Mr. Fix-it," she told him. He was told only recently that it really means "master breaker of things."

The curious Caritis kept experimenting. Turning gears and jiggling wires fascinated him. *Why isn't this working*, he thought. *Can I fix it?*

In med school, Caritis was drawn to physiology and pharmacology. Unlike microbiology or anatomy, which required mostly memorization, pharmacology explored how organs function and tested how adding one medication affected the entire human machine. He also loved the thrill of surgery, of peering inside the body and repairing it.

Caritis chose obstetrics—a unique field wherein patients seek care for a happy event in their lives—but the science of pharmacology still pulled at him. Unfortunately, there was no field to combine the two interests.

Here, Caritis saw an urgent need. "The vast majority of medications are not FDA approved for use during pregnancy," he says. And yet pregnant women take, on average, seven medications; chronic conditions don't disappear when sperm meets egg. This means that pregnant women, ever careful to avoid deli meat and unpasteurized cheese, are told to take everything from aspirin to insulin in doses that may not be optimal for them. For example, pregnancy increases bloodflow to the kidneys by 50 percent, so drugs like seizure medications, primarily eliminated by the kidneys, are eliminated twice as fast during pregnancy, meaning that these women aren't getting enough of the medication they need.

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The National Institutes of Health have long encouraged the pharmaceutical industry to fund research on pregnant women. Instead, because of the inherent difficulties in studying this population and the liability risk that remains long after birth, the industry discourages clinical trials in pregnant women.

After his residency, along with Stanley James at Columbia University, Caritis studied pregnant nonhuman primates. He performed uterine surgery to check fetal responses to interventions like labor-inhibiting medication. The work suited him, and he was good at it. In time, preventing premature labor through medication became his career specialty.

In 1975, when Caritis returned to the University of Pittsburgh as a professor in the Division of Maternal-Fetal Medicine, Department of Obstetrics, Gynecology, and Reproductive Sciences, he teamed up with Raman Venkataramanan from the School of Pharmacy. The two spent the next 30 years fighting to fund clinical research one grant at a time, testing at Magee-Womens Hospital of UPMC various medications and their effects on pre-term labor. Caritis and Venkataramanan learned which medications were effective but still weren't sure of the proper dosage for the mother or the direct effects of the medications on the placenta or fetus.

Then, in 2004, the National Institutes of Health (NIH) requested proposals from researchers looking to study various medications taken by pregnant and nursing mothers. This was the opportunity Caritis had been seeking for decades. The NIH agreed that his research interests were perfect for the project. Caritis and Venkataramanan established the University of Pittsburgh as a founding member of the Obstetric-Fetal Pharmacology Research Unit (OPRU), a multicenter network that investigates the impact of the physiological, cellular, and molecular changes of pregnancy on pharmacokinetics.

First, they studied glyburide, a medication used to lower blood sugar in women with gestational diabetes. Not surprisingly, they showed that pregnant women metabolize this drug twice as fast as nonpregnant adults; similar findings regarding labor-inhibiting medications followed. They've published multiple papers each year since the network began in *Journal of Clinical Pharmacology, American Journal of Obstetrics and Gynecology, Molecular Endocrinology*, and elsewhere.

Recently, the OPRU began studying Diclectin, a morning-sickness drug. They proved it's safe during pregnancy and also determined appropriate dosage. The medication received FDA approval in April.

As the OPRU expanded, Caritis and Venkataramanan realized they needed to recruit more scientists. In 2012, the pair earned a prestigious T-32 training grant from the NIH, bringing Pitt med what's probably the world's first postdoctoral fellowship in obstetrics and pharmacology.

Sixty years after his first dissection in his parents' kitchen, Caritis is building a previously nonexistent subspecialty in maternal-fetal medicine. Not bad for a master breaker of things. ■