

## WHY HAS THIS NOT BEEN DONE BEFORE?

This question tends to be raised by parties interested in bioZhena. The simple answer is that the folliculogenesis-tracking-via-the-cervix technology with a customer-friendly user interface resulted from a unique synergy of biomedical insight, physical science, and a need-driven quest for a solution. (This was in due course followed by recognition of the opportunity and of the broad significance.)

By the time you finish reading this brief, you should be quite comfortable with the big f word. "Folliculogenesis" stands for the cyclically or periodically recurring process of maturation of the ovum or egg. The focal point of the folliculogenesis process is ovulation, which means the expulsion of the ovum from its ovarian follicle [the root of the f word], a little protective sac within one or the other ovary. After ovulation, conception can occur for only a few hours. That is, if sperm are present in the woman's reproductive tract, fresh or at most a couple of days old, because they do not survive for too long, either.

Because our Ovulona<sup>TM</sup> sensor generates a reproducible cyclic pattern with a number of peaks and nadirs, and these are all predictably related to the ovulation marker, we can assess the beginning and the end of the brief fertile period. The older methods, all tracking certain hormones, either directly or indirectly, in certain body fluids, cannot do this. They cannot do this because those hormones are merely inputs into the complex regulatory mechanism that constitutes folliculogenesis. And the body temperature reacts to ovulation indirectly because one of the sex hormones has an effect on it.

The bioZhena folliculogenesis-tracking technology would not have arisen had it not been for those three ingredients coming together: The motivating need, the physical science (electrochemistry in particular), and the biological insight, nourished by pharmaceutical R&D practice of interdisciplinary combination of life science and physical science principles.

Folliculogenesis is a fairly esoteric biological subject, of interest to specialized biological and medical scientists. To make an understatement, you will not come across many, if any, physical scientists or technologists working with it. The concept of folliculogenesis is a fairly recent development even within biology and medicine.

Those who work with folliculogenesis do so basically - and invariably - to manipulate the female organism either to chemically interfere with or to chemically aid the occurrence of ovulation, that is to prevent or to enhance the chances of conception, respectively. We do not. We use the in vivo tracking of folliculogenesis as a handle on, a window on, reproductive health. But then, women's health generally revolves around the menstrual cycle, that is, folliculogenesis. So, we have a handle on other things, too.

We had not set out to study folliculogenesis. At the onset we just needed to anticipate and to detect ovulation. Ovulation happens to be the most important stage of folliculogenesis, and it became apparent to us only in due course that what we have been working with is folliculogenesis. Note: working in vivo, not in vitro.

Less than a century ago, two medical doctors independently <u>discovered that women can conceive only during</u> a <u>brief period</u> "in the <u>middle of the menstrual cycle</u>". They offered to women and their healthcare providers some hope with what became later known colloquially as the Vatican roulette (the calendar method of guessing at the fertile window). Since it did not work, but chemistry and science did wonders, artificial contraception came along - somewhat before the great revolution in consumer electronics. The latter produced the digital and/or further microcomputerized thermometers, for a better guess at ovulation than the primitive calendar method could. Separately came Natural Family Planning and its "sympto-thermal" method.

Then the body fluid tests, in the mistaken belief that this or that sex hormone could pinpoint the elusive brief fertile period. Not so, whether by the urinalysis LH kits or by the electronic version of same, or by electronic or visual examination of the body fluids. Those body fluid tests are peripheral reflections of what is going on, whereas we interface directly with the tissues at the organ where the action is. The cervix tissues integrate the various biological inputs, and we detect the results. Appropriately, one of our patents refers to this as endorgan effects monitoring. Concurrent monitoring for cervical tissue health is an added bonus.