The Alphabet of bioZhena

A glossary of biomedical terms for the bioZhena Corporation business plan

This glossary/primer of bioZhena Corporation is no Alphabet of Ben Sira --- an anonymous work, which has been dated anywhere from the seventh to the eleventh century, and which tells the story of the conception, birth, and early education of the "prophet" Ben Sira. There are twenty-two stories (mimicking the twenty-two letters of the Hebrew alphabet) to answer the questions posed by the Babylonian king Nebuchadnezzar. Apart from being notable for the story of Lilith, the primordial first wife of Adam, what makes this text particularly unique and fascinating is its irreverent tone … And, we get to learn of the angels who are in charge of medicine: Snvi, Snsvi, and Smnglof! For more information, go to http://www.google.com/search?q=Alphabet%20of%20Ben%20Sira !

A simple description and pictorial representation of the female reproductive organs is available at the American Medical Association's web site "Atlas of the Body: Female Reproductive Organs":
http://www.medem.com/MedLb/article_detaillb.cfm?article_ID=ZZZ8QKJ56JC&sub_cat=2

A more detailed treatment of Sexual Reproduction in Humans is given in http://www.ultranet.com/~jkimball/BiologyPages/S/Sexual_Reproduction.html .

For a particularly enjoyable, stimulating and informative source on the intimate geography of womanhood, reach for Natalie Angier's Pulitzer Prize winning book "Woman – An Intimate Geography", Houghton Mifflin Company, 1999, ISBN 0-395-69130-3. An excellent background read for the appreciation of bioZhena. But read Mysterious conceptions, under M, below.

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A

Amenorrhea:

Abnormal absence of menstrual blood flow [derived from Greek a, without + Greek men, month + -rrhea from Greek -rrhoia, a flow]. The absence or discontinuation or abnormal stoppage of the menstrual periods. This is a fairly common occurrence with causes including pregnancy, stress, loss or gain of weight, menopause, breast-feeding, anemia, excessive exercise, stopping contraceptive pill intake, some drugs, ovarian cysts or tumors, etc. The bioZhena technology will be helpful in the management of amenorrhea.

Androgens:

Steroid hormones, such as testosterone or androsterone, that control the development and maintenance of masculine characteristics. Also called androgenic hormones.

By the conventional reckoning of embryology, fetuses are pretty much primed to become female, unless the female program is disrupted by gestational exposure to androgens. If not thus disrupted, the primordial genital buds develop into a vulva and a vagina. The brain may also assume a female configuration, but this is a much more fuzzy issue.
Females are said to be the "default" sex, while males are the "activated" sex. That is, a fetus will grow into a girl in the absence of a surge of fetal androgens. The androgenic hormones organize – or, more precisely, reorganize – the primordial [primary, first in sequence, original] tissue into a masculine format.

However, this concept is not quite consistent with the notions discussed under Fetal sex pre-selection. Or is it?

Anovulation:

Absence of ovulation caused by malfunctioning HPO axis, an increasingly common problem. Presents variously as irregular menstruations, amenorrhea, and excessive facial and body hair (hirsutism). Serious consequences are infertility and a greater risk for developing gynecological cancers. The health system must manage anovulatory patients to avoid these consequences. One of the causes is obesity, which leads to overproduction of estrogens.

ART or Assisted Reproductive Technologies:

Also referred to sometimes colloquially as the "heroic procedures", they are used to treat infertility patients. ART refers to all techniques involving direct retrieval of oocytes (eggs) from the ovary. They are: artificial insemination (AI), IVF (in vitro fertilization), TET (tubal embryo transfer), ZIFT (zygote intra-fallopian transfer), GIFT (gamete intra-fallopian transfer), ICSI (intra-cytoplasmic sperm injection), blastocyst transfer and other infertility treatments, such as IUI (intra-uterine insemination), assisted hatching (AZH), and immature oocyte maturation (IOM). Web reference: http://www.ebiztechnet.com/cgi-bin/getit/links/Health/Reproductive_Health/Infertility/Education/Assisted_Reproductive_Technologies/

Atrophy:

Defined as a wasting or decrease in size of a body organ, tissue, or part owing to disease, injury, or lack of use; a wasting away, deterioration, or diminution. Any weakening or

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degeneration (especially through lack of use). Synonymous with withering; to wither, to dry up or shrivel from or as if from loss of moisture, to lose freshness; droop. From Greek atrophia, from atrophos, ill-nourished: a-, without + trophe, food. With the extremely low estrogen production in the postmenopausal age, or many years after castration, atrophy of mucosal surfaces takes place, accompanied by several problems. Those are: vaginitis (inflammation of the vagina, or the genital canal, usually of its mucous lining membrane; usually associated with candidiasis), pruritus (an intense itching sensation), dyspareunia (difficult or painful coitus, intercourse; from Greek dyspareunos: badly mated), and stenosis (a constriction or narrowing of a duct or passage; a stricture - from Greek stenosis, a narrowing, from stenos, narrow).

Candidiasis is an infection with a fungus of the genus Candida, especially C. albicans, which usually occurs in the skin and mucous membranes of the mouth, respiratory tract, or vagina but may invade the bloodstream, especially in immunocompromised individuals. Also called candidosis, or moniliasis.

Genitourinary atrophy leads to a variety of symptoms (in both sexes), which affect the ease and quality of life. Atrophy, the "conceptual junior cousin" of apoptosis (programmed cell death), is arguably the worst aspect of menopause, of the climacteric. Urethritis (inflammation of the urethra, the canal by which the urine is conducted from the bladder and discharged) and dysuria (difficult or painful urination), urgency incontinence, and urinary frequency are further consequences of mucosal thinning, in this case of urethra and bladder. Most cases of urinary incontinence can be improved by estrogen therapy, which is invariably successful in reversing the atrophic problems. Relief from these problems often results in significant improvements in general well-being.

It is known from objective measurements that vaginal factors, which influence the enjoyment of sexual intercourse, can be maintained by appropriate doses of estrogen. A significant response can be expected within a month, but it takes a long time to fully restore the genitourinary tract (6 to 12 months). Furthermore, sexual activity by itself supports the circulatory response of the vaginal tissues and enhances the therapeutic effects of estrogen, and sexually active older women have less atrophy of the vagina even without estrogen.

However, estrogen is believed to be beneficial in reducing the general age-related decline in muscular competence, with potential protective consequences against fractures, as well as the benefit due to the ability to maintain vigorous physical exercise. There is even some evidence that estrogen treatment may have a protective effect against rheumatoid arthritis, but this is debatable.

Axis:

A concept used in gynecological endocrinology in connection with the hormones that regulate the processes we are concerned with. For example, the hypothalamic-pituitary-ovarian (HPO) axis is the regulatory (feedback) system that governs menstrual cycles. In this system, which includes the brain and the reproductive tract, the brain's gland called the hypothalamus secretes the hormone GnRH, and the pituitary gland releases the gonadotropin hormones LH and FSH; in response, the ovary secretes androgens, estrogen, progesterone, and other factors. These ovarian secretory products modulate hypothalamic and pituitary output of the brain. Similarly, the hypothalamic-pituitary-adrenal (HPA) axis is the system that regulates the adrenal glands (two glands on top of the kidneys), basically as follows: the hypothalamus secretes primarily CRH (corticotropin-releasing hormone), the pituitary secretes ACTH (adrenocorticotropic hormone), and the adrenal secretes cortisol, although there are also other modulatory factors at each level. The system works through body fluids, primarily blood circulation.

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B

Barrier methods of birth control:

Contraceptive devices that block sperm from entering the uterus. These are the male and female condoms, diaphragm, cervical cap, and spermicides. Female barrier contraceptives are among the earliest recorded birth control methods (along with chemical contraceptives made of natural materials). As early as 1850 B.C., Egyptian women were advised to use a plug of certain mixtures for birth control. The first modern contraceptives were the cervical cap and vaginal diaphragm. Invented in the 1880s by a German Dr. Wilhelm Mensinga, it became popular when it was used in the world's first birth control clinic in Holland in 1882, thus earning its nickname among the English, the Dutch cap.

The vaginal diaphragm made its first appearance in the U.S. in the 1920s. Another German, Dr. Friedrich Wilde, had described the use of a rubber cervical cap. Such devices ultimately found wide usage in Europe and the United States, in various modifications and made of various materials (rubber, plastic, and metals such as aluminum or silver) as what we know today as the diaphragm. The first American patent for a pessary was by J.B. Beers, "Preventing Conception", Patent Number 4729, date of patent Aug. 28, 1846. The invention was a "curved hoop attached to a handle by a springjoint". Within a few years, The Transactions of the National Medical Association for 1864 counted 123 different kinds of pessary of every variety, from a simple plug to a patented threshing machine, and one medical observer commented, "this filling of the vagina with such traps, making a Chinese toy-shop of it, is outrageous"!

A variety of spermicidal agents have been developed since 1935. Since the 1950s, many creams and jellies have been available. They are effective even without mechanical devices such as the diaphragm, due to the bases, which spread well when warmed, and adhere efficiently to the vaginal mucosa. In addition, spermicidal agents have been incorporated into vaginal creams and jellies. Vaginal foams have been developed based on freon gas that under pressure aerates the vaginal cream. In the 1950s, before the advent of the Pill and of the IUDs, there were about 1.5 million users of vaginal contraceptives, out of the then 40 million fertile women in the U.S. (less than 4% contraceptive usage).

BBT or the Basal Body Temperature method:

A method for monitoring fertility in which women chart their temperature every morning before getting out of bed. The BBT increases after ovulation, by about two tenths of a degree. The BBT is sometimes called the waking temperature because it must be taken immediately upon awakening, before any activity, so as to signify the body temperature at rest (basal temperature). The hormone progesterone is responsible for the post-ovulation rise in the BBT, but the BBT also responds to other stimuli that cause false temperature rises, such as fever, restless sleep, antidepressants or drinking alcohol.

Billings Ovulation Method (BOM):

An NFP method in which the fertile days are identified exclusively by observations of cervical fluid at the vaginal opening. Developed by the Australian Drs. John and Evelyn Billings. An international survey in 1987 indicated that at least 50 million couples were using the method, and the number is said to be increasing from year to year. It has also been estimated that 80% of natural family planning world-wide is now the Billings ovulation method. In 1978 an

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international conference in Melbourne was attended by delegates from 48 countries. See also the cervical mucus method.

Biological rhythms and chronobiology:

A biological rhythm is any cyclic change in the level of a bodily chemical or function. For more details, see http://www.ziplink.net/~rstriker/newsltr2.htm .
A University of Texas course on MEDICAL AND PUBLIC HEALTH CHRONOBIOLOGY teaches that chronobiology is the study of biological rhythms; it is an emerging discipline in clinical medicine and public health. It addresses the influence of biological rhythms and time patterns upon human illnesses, and upon medications in their treatment. It also studies the results of altered rhythms and time schedules on shift workers. [Ref.: Congressional Office of Technology Assessment. Biological Rhythms. Implications for the Worker. U.S. Printing Office, September, 1991.]

Some chronobiological definitions are [http://www.sph.uth.tmc.edu:8053/envi/medchronodef.htm]:

BIOLOGICAL RHYTHM: A biological process or function which repeats itself and has a more or less non-varying period.
BIORHYTHM: An internally generated biological rhythm which satisfies the following criteria:
(1) repeatable in time, with the cycle duration of the repetition being fixed under normal conditions of life,
(2) phase-shiftable in the same direction and amount as the shift in the sleep-wake or environmental synchronizers, and
(3) free-running under constant environmental conditions with the removal of all known time cues.
BIORHYTHM THEORY: Pseudoscientific theory, a belief that physical, emotional and intellectual aspects are cyclic with periods of 23, 28 and 33 days, respectively, and that each is set into motion upon birth. Astrological non-science that has gained its way into industrial management and safety theory occasionally.
CHRONOBIOLOGY: The study of biological rhythms and their clocking mechanisms.
CHRONOPHARMACOLOGY: Study of biological rhythm influences on medications and other chemical agents according to the biological time of administration or exposure.
CHRONOTHERAPEUTICS: The delivery of medications or other medical treatments taking into account the programmed-in-time requirements (rhythms in disease processes: termed chronopathology).
CIRCADIAN RHYTHM: A rhythm which exhibits a period of about 24 hours (between 20-28 hours depending on environmental conditions). “Circadian” is derived from a Latin phrase meaning "about a day" [about (circa) and a day (dia)]. In humans and other mammals, a circadian clock is located in the suprachiasmatic nucleus (SCN), in the hypothalamus. The circadian clock controls longer cycles such as seasonal rhythms in reproduction, metabolism and appetite. The pineal hormone melatonin (a hormone that induces sleep) mediates this seasonality. Morningness and eveningness describe a person's individual circadian profile. Circadian rhythms can only shift an hour or two per day when a person changes his or her sleep schedule, so resynchronization takes several days [http://ergo.human.cornell.edu/studentdownloads/DEA325pdfs/biorhythms.pdf]. Different organs have their own clocks, and the most recently published one is the peripheral circadian system of blood vessels, whereby the research also shows how hormones and vitamines can reset the human circadian clock in the brain. This has a bearing on chronotherapeutics and individualization of medical treatment.
CIRCAMENSUAL RHYTHM: Rhythms which exhibit approximately 1 cycle per month.
CYCLE: Something that oscillates, with the repetitions being regular and predictable in time. Also, one cycle is one period.

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DIURNAL: A circadian rhythm that is synchronized with the day/night cycle [a Cornell University definition, better than the Houston one].
ENDOGENOUS RHYTHM: A rhythm which is driven by internal body clocks rather than reflecting environmental periodicities and their effects on the body's biochemistry or physiology.
EXTERNAL SYNCHRONIZATION: Situation when the biological time structure, particularly the staging of rhythms of each frequency class, is organized to meet predictable-in-time alterations in the external environment, e.g., activity during the day, sleep at night; etc.
FREQUENCY: The number of repetitions per unit time; it is inversely related to the period length.
HOMEOSTASIS (homeo = same or constant; stasis = state): The prevailing concept in medicine and human biology claiming the body's internal environment is maintained as a relative constant state through the actions of specific feedback "homeostatic" mechanisms.
INFRADIAN RHYTHMS: Rhythms which exhibit periodicities greater than 28 hours. While extensive research findings have been made in regards to circadian and ultradian rhythms, little conclusive evidence has been acquired on the longer infradian rhythms, which are more difficult to study.
PERIOD: The duration of time required for a rhythm to complete one cycle.
PULSATILE RHYTHM: A rhythm-like ultradian cyclic process which may not exhibit a precise period length, but which nonetheless exhibits rather dramatic temporal variability.
ULTRADIAN RHYTHMS: Rhythms which exhibit periods less than 20 hours. For example, the 90-minute cycles of REM (rapid eye movement) and non-REM sleep belong into this category.

The menstrual cycle is an example of a circamensual rhythm, with a period of approximately one month. It is therefore an infradian rhythm.

BioMeter, the:

BioMeter was the generic name we originally used for the bioZhena technology, but then we coined the name Ovulona for the human version and decided to keep the BioMeter as the name of the animal version of the technology. Although the underlying mechanism of the vaginal sensor is the same, the physical appearance and user interface are, not surprisingly, markedly different. Here, we refer to the manually used devices; the planned telemetric versions will be more similar across the species, except for the size of the permanent vaginal insert worn by the females until parturition (the birth of the offspring).

The appearance of the bovine BioMeter can be seen at http://biosense.freeservers.com/ (our old web site), which shows an industrial artist's impression of the BioMeter and of the Ovulona, both protected by our patents. Unlike the Ovulona, which is strictly a personal hygiene item for one woman only, the BioMeter has a means of identifying different animals, as the owner can monitor a group of animals with one device. The manual version of the BioMeter is intended for the breeders of small herds and/or for the breeders of individual prized animals. The electronic animal identification means enable the user to apply the device to a number of individuals whose data are stored in separate parts of the BioMeter's memory.

The importance of the BioMeter stems from the fact that timely rebreeding of the cow herd is a necessary prerequisite to profitability of beef or dairy production. Cows failing to rebreed, or rebreeding late in the breeding season, result in a 15 to 25% reduction in the potential pounds of calf weaned per cow exposed to the bull.

The significance of the BioMeter rests in its tracking of folliculogenesis, that is of the development of the ovarian follicles, which culminates in ovulation. For more details of how the BioMeter anticipates ovulation before its detection, refer to

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http://biometer.batcave.net/custom.html . No other method or technology for breeding management can do this.

The traditional criterion of optimal breeding time is the observation of the so-called standing heat (estrus). This is not good enough, which is why the livestock industry has experimented with various technological approaches, none of which has yielded a good solution, which is why the industry needs the BioMeter. The importance of the BioMeter is highlighted, for example, by reference to the Beef Herd Management Reference Binder and Study Guide of the Alberta Agriculture, Food and Rural Development, at http://www.agric.gov.ab.ca/livestock/beef/bg405-1.html . Considering the following facts from their "Physiology of the Normal Estrous Cycle" will give you an understanding of why an objective instrumental method of tracking the progress towards ovulation is essential for good breeding management.

Ovulation occurs approximately between 16 and 30 hours after the onset of standing heat. That is how uncertain is the time when the ovulatory follicle on the ovary ruptures and the egg, released into the oviduct, becomes available for fertilization. After a long-term predictive signal 10 days before ovulation, the BioMeter gives a three-day warning of forthcoming ovulation, which occurs the day after the apex of the last and large follicular wave tracked by the BioMeter.

The species that are considered to be continuous breeders (including the cow) are not without periods of anestrus, during which the estrous cycle stops. For example, anestrus is commonly observed in cows, especially young cows, when nursing calves and subsisting on low levels of nutrition.

Estrus is not always accompanied by ovulation, nor is ovulation always accompanied by estrus. Heat without ovulation (called anovulatory estrus) will not result in pregnancy if the female is bred. Anovulatory heats are common in heifers before reaching puberty, and may even be observed in pregnant cows. A heifer is a young cow that has not yet given birth to a calf. Replacement heifers make up approximately one in five females in the breeding herds of most ranches. Production of suitable replacements is an expensive process, and over 20% of all replacement heifers exhibit anovulatory estrus at some time prior to reaching puberty. The farmers and ranchers have a great economic interest in improving their breeding efficiencies.

Ovulation without the external signs of heat (called silent heat) is not uncommon in cows, especially the first few weeks after calving. All mammals lactate, as milk is necessary to support the young once it is born. During pregnancy, the mammary gland enlarges and prepares for lactation, which begins once the offspring is delivered. Generally, lactation has a suppressive effect on cyclic activity. Nursing a calf can greatly diminish displays of estrous behavior (heat). However, both horses and cattle commonly cycle when suckling a baby, and commonly become pregnant before the offspring is weaned.

The first heat after delivering a baby is called postpartum estrus. The cow and the horse can both be pregnant and suckle at the same time. They can gestate and lactate at the same time. (Unlike them, the pig can only either gestate or lactate.) Typically, the first estrous period after calving is an abnormally short estrous cycle (7 to 11 days in length, as opposed to the more common 17 to 24, with an average of 21 days). Short cycles are due to premature regression of the corpus luteum, but the causative factors are currently unknown.

Clearly, an objective method of tracking the progress towards ovulation is essential for good breeding management. The BioMeter provides for such a method. See also under Bovine, under Fetal sex preselection, under Timing of insemination, and under Modus operandi, below.

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Biosensor:

A sensor or transducer that utilizes a biochemical or biological material in the process of measurement of a physical property of the monitored system, often a concentration of a substance. It involves coupling of a biological material (for example, enzyme, receptor, antibody, organelle, whole cell, or – as with the bioZhena technology – whole tissue) with a microelectronic system or device, to enable rapid, accurate and sensitive detection. The bio-electronic coupling provides a translation of a biochemical interaction at the probe surface into a quantifiable electronic signal.

Bovine:

Of cows. Bovine data from http://www.selectsires.com/heatdet.html :
One area that surprised (and troubled) me was the number of cows being bred based on some secondary sign of heat followed by the farmer telling the technician to "palpate her and see what you think." Standing heat varies in length and intensity from cow to cow but on the average lasts about 10-12 hours. Although ovulation is triggered by the same hormonal mechanism that causes the cow to enter standing heat, it does not actually occur for another 25-30 hours. Secondary signs of estrus, including uterine tone, are stimulated by small increases in estrogen levels. In some cases, secondary signs may often be observed as much as 48 hours prior to standing heat. [Optimal] timing of insemination is [currently] accomplished by knowing initial time of standing heat. Inseminating animals 10-12 hours after first observing standing heat will allow the viable life span of spermatozoa (20-24 hours) to overlap with ovulation and the viable life of the egg (6-8 hours). Inseminating cows based on secondary signs of heat will often result in many animals being inseminated too early and the sperm life is depleted prior to ovulation. [END OF QUOTE]

C

Calendar method:

An untenable method for predicting fertility for women with regular menstrual cycles to attempt to predict their fertility by charting their menstrual cycles on a calendar. The method has been discredited because of two factors: its unwarranted assumption of regularity of menstrual cycles, and the long period of abstinence demanded by it. Also called the rhythm method, its one-time well-known status has caused a skeptical bias in America to all NFP or FAM methods, although the other methods are very different.

Cervical cancer:

Studies have indicated that the risk of dysplasia and carcinoma in situ of the uterine cervix increases with the use of oral contraceptives (OCs) for more than a year. Invasive cervical cancer risk may be increased after 5 years of use, reaching a two-fold increase after 10 years. Another study concluded that women who used oral contraceptives for between five and nine years were about three times more likely to have cervical cancer; those who were on the Pill for 10 years or more were at four-fold increased risk. Also, HPV-infected women who have had five or more children were also found to be at increased risk of cervical cancer. HPV stands for the human papilloma virus, a sexually transmitted virus that is the major cause of cervical cancer.

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It is well recognized, however, that the number of partners a woman has had, and the age at first intercourse, are the most important risk factors for cervical neoplasia. Complicating factors include exposure to the human papilloma virus, the use of barrier contraception, and smoking. These factors have made conclusions about cervical cancer difficult, and the CDC has once concluded that there is no increased risk of invasive cervical cancer in users of oral contraception, and that an apparently increased risk of carcinoma in situ is due to the enhanced detection of disease (because oral contraceptive users have more frequent Pap smears). Another study has found that there is a minimal risk for invasive squamous cell carcinoma but a significantly increased risk for invasive adenocarcinoma. This concern is an important reason for annual Pap smear surveillance, and it is considered reasonable to perform the Pap smears every 6 months in women using OCs for 5 years or more, who are also at higher risk because of their sexual behavior [e.g., multiple partners and history of STDs]. Studies have shown that the sexually promiscuous woman at all ages has an increased risk of developing cervical neoplasia; this risk seems to be the highest in the third decade of life. Cervical cancers typically grow slowly, so regular surveillance can catch the cancer early — often, when cells are just beginning to turn cancerous. Six in 10 women who die of cervical cancer have not had a Pap test in the last five years.

According to the Centers for Disease Control and Prevention (the CDC of the US DHHS), cervical cancer is nearly 100 percent preventable, yet an estimated 13,000 new cases of invasive cervical cancer are diagnosed annually, and about 4,400 women die of the disease in the US each year. "The good news is that cervical cancer is preventable and curable if it is detected early" [http://www.cdc.gov/cancer/nbccedp/info-cc.htm].

In many countries, cervical cancer is the most common cause of cancer death among women, and "reducing cervical cancer deaths in developing countries will require new public health approaches" [Medscape Women's Health 6(6), 2001 at http://womenshealth.medscape.com/Medscape/WomensHealth/journal/2001/v06.n06/wh1206.blum/wh1206.blum-01.html].
The word "squamous" is defined as resembling a scale or scales; thin and flat like a scale. Dictionary.com's example: the squamous cells of the cervix. (For more information about cervical cancer, you can explore the web site of the National Library of Medicine at http://www.nlm.nih.gov/medlineplus/cervicalcancer.html .)

Clearly, our planned adaptation of the BioSense technology for a personal routine self-monitoring for early warning of cervical cancer is a very worthwhile endeavor. Note that the most important feature of any diagnostic screen is the screen's use on a routine basis. With our vision of the Ovulona in the purse of every woman, BioSense should make a significant impact on global public health. This aspect of the project should not escape our readers' attention, similar to the expected impact on the prevalence of STDs, both of which go beyond – and stem from - the primary purpose of personal monitoring of fertility status.

The rationale for our speculative expectation may be intuited from the understanding of the various other entries, below. Basically, it comes down to a simple notion: The Ovulona is a tissue-biosensor. If tissue goes haywire, you'd expect to see that reflected in the biosensor's response. Either the aberrant response to disease overrides the normal response to reproductive hormones with sufficient sensitivity, or we shall have the microprocessor track the health vs. disease status concurrently with the normal monitoring of fertility status. (This can be done at very little cost, and performed in the background, without any complication to the user.)

Cervical cap:

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A firm rubber cap intended to fit securely on the cervix. Used with contraceptive jelly, the cervical cap is a barrier method of birth control that is reversible and available only by prescription.

Cervical mucus:

The fluid secreted by the inner walls of the cervical canal and exuded by the cervix. The amount and the properties of the fluid change depending on the phase of the menstrual cycle, e.g., from practically nonexistent during the so-called dry days early in the cycle to the relatively copious amounts of clear slippery fluid during the fertile days. Cervical mucus is essential for the ability of the sperm to function properly: sperm survival and sperm transport within the woman's reproductive system are critically dependent upon the presence of a healthy mucus. To quote a noted expert, Professor Erik Odeblad: "Complications arising from the use of the Pill are very frequent. Infertility after its use for 7-15 years is a very serious problem. S crypts are very sensitive to normal and cyclical stimulation by natural oestrogens, and the Pill causes atrophy of these crypts. Fertility is impaired since the movement of sperm cells up the canal is reduced. Treatment is difficult." He also wrote: "After 3 to 15 months of contraceptive pill use, there is a greater loss of the S crypt cells than can be replaced … A pregnancy rejuvenates the cervix by 2-3 years, but for each year the Pill is taken, the cervix ages by an extra year." Web reference: http://www.billings-ovulation-method.org.au/act/pill.html .

Cervical mucus method:

A method of determining a woman's fertility by observing changes in her cervical mucus. The Billings ovulation method and the Creighton model ovulation method are both cervical mucus methods.

Cervical palpation:

Feeling the cervix with the middle finger of the thus trained woman-user of FAM or NFP to determine cervical position. This is not a widely used procedure, and is not involved in the Billings and Creighton ovulation methods.

Cervical position:

Three facets of the cervix (its height, softness and the size of its opening, the cervical os) assessed for fertility significance by specially trained users of this method of NFP or FAM.

Cervix:

The narrow lower part of the uterus (womb), with an opening that connects the uterus to the vagina. It contains special glands called the crypts that produce mucus, which helps to keep bacteria (and other microbes, including sperm for most of the cycle) out of the uterus and beyond. Sometimes called the neck of the womb, it protrudes into the vagina. The region around the cervical protrusion is known as the vaginal fornix. The sanitary vaginal tampon is inserted so as to reach into the posterior fornix. Likewise the bioZhena sensor. The cervix is the gateway to the uterus and has a lot of challenging roles. It must allow the passage of either sperm (or penis, in some species) at copulation, prevent the entrance of microorganisms before and particularly during pregnancy, and expel the neonate and placenta at parturition (birth). It is a muscular tube that has a very dynamic role in both the menstrual cycle and in forming a tight seal during pregnancy, but opening to form a broad passageway at birth. The

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multitude of physiological roles of this gateway has caused it to become an important element or focus of the bioZhena technology.

Climacteric:

The time of change that leads to menopause. The physiological midlife changes for women and men. See also under Atrophy, under Hot flushes (or flashes), under Menopause, and under Osteoporosis.

Colposcope:

A viewing instrument with a bright light and magnifying lens that is used to examine the vagina and cervix stained with special solutions. Colposcopy: Examination of the vaginal and cervical epithelia by means of a colposcope. [Greek kolpos, vagina, womb + -scopy, suffix that signifies viewing; seeing; observation: as in microscopy. From Greek -skopi, from skopein, to see.] Colposcopy is the diagnostic test to evaluate patients whose Pap smear screening produced abnormal cytological smear results. For more details see http://lib-sh.lsumc.edu/fammed/atlases/colpoat.html .

Combined oral contraceptives:

Birth control pills that contain the hormones estrogen and progestin (progesterone). See Pill, the: for more details.

Conception:

The moment when the pre-embryo attaches to the lining of the uterus and pregnancy begins; the term is also used to describe the fertilization of the egg.

Condom:

A sheath of thin rubber, plastic, or animal tissue that is worn on the penis during sexual intercourse. It is an over-the-counter, reversible barrier method of birth control, and it also provides some, even if not perfect, protection against sexually transmitted infections. The pregnancy rate is 5 – 15%. See also female condom.

Contraception:

The prevention of pregnancy; birth control.

Contraceptive creams and jellies:

Substances containing spermicide, which immobilizes sperm, preventing it from joining with the egg; used with diaphragms or cervical caps. These are over-the-counter, reversible barrier methods of birth control.

Contraceptive film, foam or suppository capsule:

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Inserted deep into the vagina, they contain a spermicide to immobilize sperm, preventing it from joining with an egg; over-the-counter, reversible barrier methods of birth control. Most effective when used with a condom. The film is a square of tissue that melts into a thick liquid and blocks the entrance to the uterus. The foam blocks the entrance to the uterus with bubbles. The suppository is a solid that melts into a liquid.

Corpus luteum:

The yellow gland in the ovary formed by the ruptured follicle after ovulation. If the released egg becomes fertilized, the corpus luteum supports the early pregnancy (by continuous production of progesterone). If fertilization does not occur – a much more likely eventuality – the corpus luteum degenerates in time for the menstrual bleeding.

Creighton model ovulation method:

An NFP method of vaginal-cervical mucus self-evaluation according to criteria developed by Thomas Hilgers, M.D. at St. Louis and Creighton Universities. The criteria are called the vaginal discharge recording system (VDRS) and require that women check for the mucus by wiping the outside of their vaginas with bathroom tissue, checking the mucus for color, stretch and consistency. The last day of mucus that is either clear on appearance, stretches an inch or more, and/or causes the sensation of lubrication is called the peak mucus day. The method is similar to the Billings ovulation method.

D

Depo-Provera®:

A progestin hormone (synthetic progesterone) that is injected into the buttock or arm every 12 weeks to prevent pregnancy. It is a reversible method of birth control available only by prescription.

Diaphragm:

A soft rubber dome intended to fit securely over the cervix. Used with contraceptive cream or jelly, the diaphragm is a reversible barrier method of birth control available only by prescription.

Dystocia or calving difficulty:

Dystocia is difficult delivery or parturition. From Latin dys-, bad, from Greek dus-, ill, hard + Greek tokos, delivery. Calf losses at birth result in a major reduction in the net calf crop. Data show that 60% of these losses are due to dystocia (defined as delayed and difficult birth) and at least 50% of these calf deaths could be prevented by timely obstetrical assistance. The USDA web site http://larrl.ars.usda.gov/physiology_history.htm indicates that an electronic calving monitor is being developed to determine maternal and fetal stress during calving. These studies are important since they are leading the way for developing methods to reduce the $800 million calf and cow loss that occurs each year at calving in the USA's beef herds. The telemetric version of the BioMeter will provide a tool for these efforts.

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E

Egg:

The reproductive cell in women; the largest cell in the human body. The female gamete; an ovum. Also called egg cell.

Embryo:

The embryo is the organism that develops from the pre-embryo, and begins to share the woman's blood supply about nine days after fertilization. Approximately one-half of all human embryos are abnormal
[http://www.columbialabs.com/html/crinwom/infertility/fertilization.htm]. "There is fortuitously a biologically based selection bias against abnormal human embryos. A signal is obviously recognized by the mother, which helps explain why so many embryos fail to implant. An abnormal embryo that manages to implant is often miscarried in the first 10 weeks of pregnancy. Early miscarriages are almost always the result of abnormal development of the fetus. This is why progesterone is not usually recommended for threatened abortion. It is only if the physician can confirm, using ultrasound, that the fetus is viable, will he prescribe progesterone to help maintain the pregnancy."

Emergency contraception:

The use of oral contraceptives (OCs) or IUDs (intrauterine devices; see respective entries, below) to prevent pregnancy after unprotected intercourse. These OCs are referred to as Emergency Contraceptive Pills (ECPs). Emergency contraceptives are methods that prevent pregnancy when used shortly after unprotected intercourse. Three different emergency contraceptive methods are available in the United States. These are: (1) ordinary combined oral contraceptives, containing ethinyl estradiol and levonorgestrel, taken in a higher dose for a short period of time and started within a few days after unprotected intercourse; (2) levonorgestrel-only tablets used similarly; and (3) copper-bearing intrauterine devices inserted within approximately 1 week after unprotected intercourse. The current treatment schedule for the OCs is one dose within 72 hours after unprotected intercourse (i.e., before the fertilization "takes"), and a second dose 12 hours after the first one.

A recent study by the World Health Organization found that effectiveness declined significantly with increasing delay between unprotected intercourse and the initiation of treatment. The WHO has also concluded that "the only absolute contraindication to the use of combined ECPs is confirmed pregnancy, simply because ECPs will not work if a woman is [already] pregnant… Emergency contraceptive use is best known for women who have been raped, but the methods are also appropriate for women who have experienced condom breaks, women who did not use any method because they were not planning on having sex, or women who had unprotected intercourse for any other reason". For further details, see
http://www.medscape.com/viewarticle/421029 .

Under "Barriers to More Widespread Use of Emergency Contraception", the article states: The lack of a product specifically packaged, labeled, and marketed as an emergency contraceptive was a major obstacle to more widespread use of emergency contraception in the United States until the fall of 1998, when Preven™ was approved. More recently, a second specially packaged emergency contraception, Plan B®, was also approved. Although availability of these products has helped, the two pharmaceutical companies backing them are very small and have not been

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able to promote the products on the same scale as most contraceptives. For this reason, and because the dedicated products can cost more, off-label, evidence-based use of regular ongoing oral contraceptive brands remains popular [END OF QUOTE].

The ECP emergency contraception falls within the concept of acute (as opposed to chronic) use of oral contraceptives, proposed by at least one of the people responsible for the OC phenomenon (to minimize the interference with natural hormones, and the side effects; see under the Pill). Emergency contraception is considered especially important for outreach to the more than 3 million US women who are at risk of pregnancy but who are not using any regular contraceptive method, and to the 8 million women who rely on condoms for protection against pregnancy, the latter in case of condom slippage or breakage. This market segment is clearly an early marketing target for BioSense Corporation, over and above the global market of existing NFP users [NFP, Natural Family Planning]. A suitably formulated strategic alliance with appropriate pharmaceutical firms, and with the OC-biased medical establishment, is one logical route for turning a powerful competing adversary into an ally.

Endocrinologist:

A specialist in the functioning of hormones.

Endometrium:

The lining of the uterus that develops every month in order to nourish a fertilized egg. The lining is shed during menstruation if there is no fertilization.

End-organ effect:

A concept of biomedicine, which has to do with monitoring of the effects of stimuli, usually chemical stimuli such as drugs, on a biological system, that is either a part of or the complete body of an animal, or a human subject. While the fate of a chemical compound can be monitored by detecting it in body fluids (blood, urine, saliva, etc.), it can also be monitored by measuring the effect on a certain part of the body, called the end organ because the stimulus ends up there. The same applies to stimuli and reactions that the body generates by itself. BioSense explores electronic monitoring of end-organ effects.

Equine:

Of horses. Equine data from :
http://muextension.missouri.edu/xplor/agguides/ansci/g02790.htm :

QUOTE: The sperm life in the mare's tract is from 24 to 48 hours. Only in highly irregular or exceptional cases does it exceed this time span. Sperm has been found in the Fallopian tube 15 to 18 minutes after coitus, but the normal time to travel from the site of deposit to the Fallopian tube is five to eight hours. The average egg life is also only five to eight hours.

Because of a long estrous cycle and short life span of the spermatozoa and egg, it is not uncommon to have a lower than 50 percent conception rate. Variation in the length of estrus from three to eight days is considered normal.

Ovulation usually occurs about 24 to 48 hours before cessation of visible signs of heat. Since neither the egg nor spermatozoa live long individually at body temperature, time of breeding relative to egg release is critical. There is little wonder that low settling percentages result from

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the practice of "noticing signs of heat," taking the mare to the stallion, and returning her to pasture for the rest of the season. [END OF QUOTE]

Based on the quoted parameters, it is clear that the introduction of the ovulation predicting and detecting BioMeter should make a significant impact on the horse breeding results.

Estrogen:

A hormone commonly made in women's ovaries. It is one of the primary hormones, which control the menstrual cycle. Periodically increasing estrogen levels in the first part of the menstrual cycle produce significant changes in the cervical fluid and the cervix, which are indicative of the fertile state near the day of ovulation. Actually, it is estradiol, the principal and most potent estrogen, which is "the product of the ovaries. It flows out of the cells of the follicles and from the corpus luteum, the yellow matter that forms like a blister on a ruptured follicle…"

The other estrogens are estriol and estrone. "Estriol is generated by the placenta and to a lesser extent by the liver. It is the major 'pregnancy estrogen', the source of any charming gestational glow you might have – says Ms. Angier – if you aren't green with nausea… The placenta also synthesizes estrone. So too does adipose tissue. Fat women often are spared overt symptoms of menopause such as hot flashes, and covert ones such as thinning bones; even as their ovaries cease the monthly efflux of estradiol, their peripheral tissue compensates by manufacturing estrone… For any postmenopausal woman who forgoes patches or conjugated extracts of horse piss, estrone will be the predominant estrogen until departure. Estrone alone for the merry crone."

Estrogen is called the female hormone, which is – in the words of Natalie Angier ("Woman", page 185) – "partly inaccurate and partly reasonable. From the age of twelve through fifty, women have three to ten times more estrogen circulating through their bloodstream than men do. In middle age, men and women become closer estrogenic kin, for not only do a woman's levels of the hormone drop, but a man's gradually rise. Keep in mind that, regardless of whose hormones are under scrutiny, the concentrations are vanishingly small, measured in laboratory tests in nanograms or picograms – billionths or trillionths of a gram. To obtain one teaspoon of estradiol [the most important estrogen], we would need to drain the blood of a quarter million premenopausal women. By contrast, the blood supply of any one of us contains at least a teaspoon of sugar and several tablespoons of salt…

This is a lesson learned only recently, that the body makes and consumes estrogen globally. During the golden age of hormone research, scientists thought that they did not need to look beyond the gonads: the ovaries made estrogen, the testes made testosterone. Hence the term sex steroids. They thought that the gonads made sex steroids to do sexy things, or rather reproductive things – to control ovulation, for example, and thicken the uterine lining. But no, estrogen's role is not limited to good breeding. The body makes estrogen everywhere, and the body eats estrogen everywhere."

Yet another reason why it is a good idea to explore the end-organ effects of the hormones that matter in the regulation of fertility. See End-organ effect, above, and Modus operandi, below.

Estrus:

The periodic state of sexual excitement in the female of most mammals, excluding humans, that immediately precedes ovulation and during which the female is receptive to mating. Also called heat. [From Latin oestrus, frenzy, gadfly, from Greek oistros.] Ovulation occurs towards

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the end of the estrous period. An anestrous animal is not in heat and cannot be fertilized. As the renowned endocrinologist, Professor James Brown, points out: "In animals, Nature has ensured a maximum fertilization rate (but not 100%) by restricting intercourse to the most fertile day[s] of their cycle by the phenomenon of oestrus." British spelling of estrus is oestrus.

Another interesting thing is that, in terms of timing of cyclic events, there is a certain correspondence between estrus (heat) and menstruation. Lysis of the corpus luteum (luteolysis) occurs at the end of the reproductive cycle due to prostaglandin release from the uterus, and it causes a rapid fall in progesterone as the corpus luteum ceases to function. This is followed by menstruation in primates, and by heat in non-primates. The classical difference between the menstrual and estrous cycles is that in humans and primates the endometrium is shed, whereas in animals with estrous cycles it is not. However, during the estrous cycle, vascular changes occur in the endometrium, which are not unlike those occurring in the uterus of humans and primates. Lysis means the dissolution or destruction of cells (such as blood cells or bacteria) caused by the action of a specific lysine (or agent) that disrupts the cell membrane; in the case of luteolysis, the prostaglandin released by the uterus is the lysine.

F

Fallopian tube:

One of two narrow tubes that, after ovulation, carries the egg from one of the two ovaries to the uterus. Also referenced as oviducts, or tubae uterinae, they are so called after Gabriele Falloppius, or Fallopio, a physician of Modena, who studied medicine at Ferrara and later at Pisa. Born in Modena, Italy, in 1523, in 1551 he succeeded Columbus as Professor of Anatomy and Surgery in Padua, and also occupied the Chair of Botany. Made many important discoveries, one of them being that of the bony labyrinth of the ear. Added much to the knowledge of the reproductive system. Died in 1562 or 1563.

The two fallopian tubes are attached to the upper part of the uterus on either side, and are about 4 inches (10 cm) long. They are about as thick as a piece of spaghetti. Each tube forms a narrow passageway that opens like a funnel into the abdominal cavity, near the left and the right ovary. The ends of the fallopian tubes are draped over the two ovaries and they serve to catch the ovulated egg, for the egg to travel into the uterus. Each fallopian tube is lined by millions of tiny hairs (called the cilia) that beat rhythmically to propel the egg forward. The fallopian tube is not just a pathway - it performs other functions too, including nourishing the egg and the early embryo. Also, the sperm fertilize the egg in one of the fallopian tubes.

The Professor Renaldus Columbus mentioned above was, of course, different from the seaman Christopher Columbus and, according to some of the incredibly plentiful sources on the web, he argued with Gabriel Fallopius over which of the two of them was the discoverer of the clitoris! But that would be a different story, as would be the one about Fallopius having been an avid experimenter with or the inventor of the condom – not for contraception but for disease prevention, at a time (circa the 14th to 17th centuries) when educated Europe was much concerned with these matters, "often with the explicit consent of the Church" [http://groups.google.com/groups?q=Renaldus+Columbus&hl=en&rnum=4&selm=33CFA67C.2781E494%40aztec.asu.edu]. Columbus, apparently, also coined the word "vagina".

Since bioZhena is an American enterprise, let the reader be aware that Miloš Forman (the New York-based director of Amadeus, and of One Flew Over the Cuckoo's Nest, inter alia) is talking about making a motion picture about the two renaissance anatomists. But we do not know yet whether the plan is to base the soundtrack on the music of the not-completely-unknown New

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York City and Spillville, Iowa composer Antonín Dvořák! [Forman, pronounce for – mun, from Old Czech, for wagoner, one who conducts a wagon; one whose business it is to drive a wagon, wagon-meister, definitely of the horse-drawn era. Dvořák, with the unpronouceable accented consonant, something like "rzh", again from Old Czech, for somebody courtly, perhaps courtier? Renaissance, French for the humanistic revival of classical art, architecture, literature, and learning that originated in Italy in the 14th century and later spread throughout Europe, roughly up to the end of the 16th century, marking the transition from medieval to modern times. From Vulgar Latin renascere, to be born again.]

Fecundability and fecundity:

Fecundability is the probability of achieving pregnancy within one menstrual cycle (about 20% or maybe 25% in normal couples). Fecundity is the ability to achieve a live birth. Fecundability is strongly influenced by the age of the partners, and it is maximal at about age 24. There is a slight decline at ages 24 – 30, and a rapid decline after age 30. [The words are derived from Latin fecundus, fecund, from the root of fetus, via Old French fecond.] Fecund means fruitful in children, or prolific.

Female condom:

A polyurethane sheath with flexible rings that is inserted deep into the vagina like a diaphragm. It is an over-the-counter, reversible barrier method of birth control that may also provide protection against sexually transmitted infections.

Fertile phase or fertile window:

The days of the menstrual cycle, during which sexual intercourse or insemination may result in pregnancy. It includes several days leading up to and including ovulation. The exact number of the fertile days is not known. It is currently believed to be 6 days, although evidence shows that there are only 3 days of high probability of conception (while the other three days are likely due to inadequate methods of ovulation monitoring used in earlier studies). The unequivocal determination of the fertile window is a pivotal task for bioZhena. The fertile window is an empirical factor, which should be consistent with the fertilizable lifetimes of the gametes (the egg and the sperm). Those are also uncertain but currently accepted figures are up to 12 (or maybe 24) hours for the egg, and at most 3 days for the sperm.

Fertility:

The female of any mammalian species, including the human female, can conceive only during a limited period of time (a window of a few days), and only if all conditions are perfect. The fertile window occurs repeatedly at intervals, which are more or less regular (28 + or – 9 days or so) but their variability is substantial to the extent that planned pregnancy is a challenge. A normal healthy couple will statistically take at least 3 or 4 months to conceive, even if the concept of the fertile window is known to them. An increasing percentage of couples experience difficulties in achieving pregnancy, and reproductive specialists have found that a large percentage of women had no idea of when they could conceive.

FAM (fertility awareness method):

A method of determining a woman's fertility status through self-assessment of certain fertility signs: waking temperature (also called the basal body temperature or BBT), cervical fluid, and

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cervical position. While NFP users abstain, FAM users apply one of the barrier methods of contraception for vaginal intercourse during the "unsafe days" of a woman's fertile phase.

Fertilization:

The joining of an egg and sperm. More accurately, fertilization is the union of a spermatozoal nucleus, of paternal origin, with an egg nucleus, of maternal origin, to form the primary nucleus of an embryo. It is the fusion of the hereditary material of two different sex cells, or gametes, each of which carries half the number of chromosomes typical of the species.

Although sperm can swim several millimeters per second, their trip to and through the fallopian tubes is assisted or facilitated by muscular contraction of the walls of the uterus and the tubes. There is also evidence that the egg releases a chemical attractant for sperm. In any case, sperm may reach the egg within 15 minutes of ejaculation. The trip is also fraught with heavy mortality. An average human ejaculate contains several hundred million sperm but only a few hundred complete the journey. And of these, only one will succeed in entering the egg and fertilizing it. Fertilization begins with the binding of a sperm cell to the outer coating of the egg (called the zona pellucida). Enzymes, released by the acrosome at the tip of the sperm head, digest a path through the zona and enable the sperm to enter the cytoplasm of the egg.

For fascinating details, explore the developmental biology site http://zygote.swarthmore.edu/chap4.html . You will see, e.g., a photo showing the "sun in the egg": the microtubules (stained with fluorescent antibodies to tubulin) radiating from the centrosome associated with the male pronucleus and reaching towards the female pronucleus. "This vivid image conveyed the discovery of the moment at which a new life was formed. The metaphor expressed awareness that the force of natural powers was greater than the sum of two cells."

Then, you can read up on Homunculus: Historiographic Misunderstandings of Preformationist Terminology, an essay by Clara Pinto-Correia, abstracted from her forthcoming book, The Ovary of Eve. This essay examines the association of the term "homunculus" with the "little man" that some of the leading spermists located inside the head of the spermatozoon during the rise of theories of reproduction in the seventeenth century. You can further find out that there is "a history of speculation about sex determination that views women as incomplete males… about the notion that women are almost-men whose development or evolution is truncated… how textbooks claimed that maleness means mastery, the Y-chromosome over the X, the medulla over the cortex, androgen over estrogen…"

Fetal sex pre-selection:

Here is the underlying principle: Out of the 46 chromosomes (23 pairs), the last pair is the sex chromosome. It is of the XX type in the female and XY type in the male. The ovum (egg) has X type chromosomes only, while 50% of the sperm have X chromosomes and 50% have Y chromosomes. If an X sperm fertilizes the egg, this results in an XX combination, which is a female offspring. If a Y sperm fertilizes the egg, the result is an XY combination and a male child.

According to http://www.fertility-docs.com/fertility_gender.phtml , "the selection of gender has been a quest of couples for as far back as recorded history allows. Early drawings from prehistoric times suggest that sex selection efforts were being investigated by our earliest ancestors. Later history shows intense interest in sex selection by early Asian (Chinese), Egyptian and Greek cultures. This is followed by documented scientific efforts beginning in the 1600s to sway the chances of achieving a pregnancy by a variety of methods…"

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Two approaches to sex selection have been demonstrated in the current scientific literature. One approach employs the tools and methods of assisted reproductive technologies (ARTs), manipulating the genetic material of the sperm prior to artificial insemination, so as to facilitate fertilization by the selected one of the two genders of the spermatozoa. The other approach attempts to enhance the probability of conceiving the desired gender by appropriate timing of the conception event with respect to ovulation. This is a highly controversial subject despite the fact that a substantial body of work on it has been published.

Thus, a 2001 publication by respected experts from a premier infertility treatment institute (G.Hodgen et al.) has put forward evidence that male spermatozoa (Y-chromosome-bearing sperm) live longer than female spermatozoa (X-chromosome-bearing). This is consistent with earlier findings by Auckland, New Zealand researchers that boys tend to be conceived earlier in the fertile period than girls (the earlier conception requires a longer lifetime of the sperm). A 1991 Johns Hopkins University meta-analysis of six NFP studies concluded that the data showed "a statistically significant lower proportion of male births among conceptions that occur during the most fertile time of the cycle", meaning near ovulation. Indeed, the Auckland study by Professor John France's group found that 65% of male infants were conceived 2 to 5 days before ovulation while "71% of the born girls were conceived from intercourse timed between 1 day before to 1 day after the estimated time of ovulation".

A similarly high level of interest in embryo sexing (fetal sex pre-selection, or sex ratio) exists in the livestock industries, and researchers have experimented with the timing of insemination method. A tool such as the bioZhena Corporation's BioMeter is indispensable for this approach to embryo sexing, because of the required accuracy and precision of the timing. The controversy in the veterinary literature is a clear evidence that timing the insemination merely with respect to estrus is not good enough. The timing must be with respect to ovulation. The BioMeter, which detects ovulation as well as anticipating it, should make it possible to investigate questions such as whether different species have different lifetimes of the sperm. It should be possible to establish what kind of a distribution of sperm lifetimes there may be within a species. (See also under Timing of insemination.)

The 2001 book Biotechnology in Animal Husbandry (R. Renaville & A. Burney, editors, Kluwer Academic Publishers) has a chapter on Sex Preselection in Mammals. The abstract states: Since a long time, sex preselection has been a goal of the dairy and meat industry to increase the rate of response to selection, to reduce the cost of progeny [offspring or descendants] testing for elite males, and to produce desired specialized and genetically superior offspring. The authors write: In animal husbandry, pre-selection of sex prior to conception will dramatically impact a farmer's productivity and income, because in each of the chosen target industries there is a strong preference for one sex over the other. For example, the dairy industry must have females to produce milk whereas the beef industry prefers males for their higher quality and lower cost of production. Sex preselection is one of the most sought after biotechnologies of all times.

In a section on Factors Affecting Sex Ratio, the experts write: Considerable folklore particularly in humans has arisen regarding preconception methods to manipulate animal sex ratio. The authors point out that conventional wisdom holds that steroid hormones play no role in sex predetermination in mammals, and it is only after gonadal differentiation that steroids sculpt the characteristics, which distinguish males from females. They also write that, for a number of years, the time of insemination or mating during estrus has been believed to influence the sex ratio of offspring, and they review various conflicting reports in several animal species. One kind of these results, in cows, indicates that the sex ratio may be affected by the maturational state of the oocyte [egg] at the time of insemination (yielding sex ratio 0.7 when inseminated immediately after, and 2.5 when inseminated 8 hours after polar body extrusion, which

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basically means ovulation). In their Conclusion, the experts again point out that "economics dictate that livestock producers are under increasing pressure to produce a given number of progeny of the desired sex."

The results of sex pre-selection experiments depend on the state of the ovulating egg and the sperm. This may depend on whether a given father belongs into a sub-population of males with long or short sperm lifespan. Whether there is such a thing as this kind of categorization within a species can only be established by means of a tool such as the BioMeter. This holds for all species, including Homo Sapiens, of course, and public health statistics make such categorization actually quite likely. In the U.S., the sex ratio (number of males born per 1000 females) has declined from 1.052 in 1983 to 1.049 in 1999, having been as low as 1.047 twice in the late nineties. Interestingly, this decline is evidently due to the decline in the white race (from 1.057 to 1.052, through as low as 1.049) whereas for the black race the sex ratio has actually increased over those years (from 1.028 to 1.031, through as high as 1.036) [web reference: http://www.infoplease.com/ipa/A0005083.html]. All this is clearly suggestive of a likely strong reason why people will want to use the bioZhena products, and the application will not even need to be advertised.

Fetus:

The organism that develops from the embryo at the end of about seven weeks of pregnancy and receives nourishment through the placenta. Fetus, plural fetuses: 1. The unborn young of a viviparous vertebrate having a basic structural resemblance to the adult animal. Viviparous: Giving birth to living offspring that develop within the mother's body. Most mammals and some other animals are viviparous. Vertebrates have a backbone or spinal column. 2. In humans, the unborn young from the end of the eighth week after conception to the moment of birth, as distinguished from the earlier embryo. [From Latin fetus, offspring.]

Follicles:

Small fluid-filled spherical structures in the ovaries that contain the eggs. At ovulation, the matured dominant follicle (grown to about an inch in size) ruptures the surface of the ovary and releases the egg, which is sucked into the fallopian tube so as to be propelled towards the uterus. Upon the egg-release, the follicle becomes luteinized (changes into a yellow "body" or corpus luteum) and starts producing progesterone.

FSH or follicle stimulating hormone:

The hormone produced by the pituitary gland in the brain that stimulates the ovaries to produce mature ova (eggs) and the hormone estrogen.

G

Gametes:

The reproductive cells — eggs and sperms. [From Greek gamete, wife, and gametes, husband, from gamein, to marry, from gamos, marriage.]

Gestation:

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The period of development in the uterus from conception until birth. The act of carrying young in the womb from conception to delivery, i.e., pregnancy. [Gestation is from Latin gestatio: a bearing, carrying, from gestare to bear, carry.] Since the expression is also linguistically related to the word jest, we observe that a now-obsolete meaning is also the act of wearing clothes or ornaments. And if that is not enough, it also once meant an exercise in which one is borne or carried, as on horseback or in a carriage, "without the exertion of one's own powers", i.e., passive exercise. Joking aside (extra jocum, remotum joco, as the Latin speaker would say), the gestation period is the period during which an embryo develops, the length of time between fertilization of an ovum and parturition (birth).

MedTerms.com also advises that for humans the full gestation period is normally 9 months. Which is where the experts' (not the women's!) fun begins because the reference is to lunar months, the average time between successive new or full moons, equal to 29 days, 12 hours, 44 minutes, 2.87 seconds. Also called synodic month. Lunar month is the period of one revolution of the moon, particularly a synodical revolution; but several kinds are distinguished etc., etc., etc.

One concerned obstetrician, Dr. David J. R. Hutchon, teaches [http://www.obgyn.net/us/cotm/9807/cotm_9807.htm]: "Aristotle, the father of scientific thinking, wrote that there was a certain definite term of gestation for all animals, which varied from animal to animal according to its size and life expectancy. However in man, wrote the philosopher, 'the human foetus is expelled both in the seventh and the tenth months, and at any period of pregnancy between these; moreover, when the birth takes place in the eighth month, it is possible for the infant to live.' " Hutchon confirms this with hard data, in a scattergram that "shows a good fit between 37 and 42 weeks". He also tells us that it was Harmanni Boerhaave - a botanist who read in the Bible that pregnancy should last 10 lunar months - who in 1744 formulated a way of calculating the expected date of delivery. The rule was later given publicity by Franz Naegele in 1812, for whom the 40 weeks or 10 lunar months rule is named today. However, "Boerhaave was not actually measuring the length of pregnancy, and the word 'gestation' is used to describe the measurement of time from the last menstrual period to reflect this, so … there is no pretence that this method is determining fetal age."

In the December 2001 issue of Obstetrics and Gynecology, a team of physicians proposes that "patients be given an assigned week of delivery at 32 weeks' gestation, individualized for each clinical situation. For most pregnancies, the assigned week of delivery might be between 39.5 and 40.5 weeks' gestation." According to these obstetricians, "the problem is that the term 'due date' has caused tremendous anxiety and tension over the last 3 decades … [and] clinicians literally spend more time explaining why a person isn't really due on their due date than [they] spend on testing for AIDS, neural tube defects, and high blood sugars, and explaining what labor is like."

The referenced obstetricians do not draw any parallel between Aristotle's observation of the difference between animals and Homo Sapiens and the difference between the animals' estrus and the human freedom from it (see the Estrus entry, above). Just as with the baroque-era Boerhaave, the modern obstetricians' approach is not concerned with the length of the menstrual cycles or the certainty of the dates. Yet, it is evident that the EDD can be projected quite well from the ultrasonic measurements of the unborn baby's head, which could solve the anxiety and tension problems of prospective mothers – if the obstetricians chose to. While the expectant mother could not perform such ultrasonic measurements by herself, even if she wanted to, it will be interesting to see if bioZhena can provide a simple alternative of better EDD assessment. The details of the gestation process are represented at Discovery.com's "The Visible Embryo", http://www.visembryo.com/baby/index.html . Also, see http://www.paternityangel.com/PicsAndPhotos/FoetalDevelop/DevInPics.htm for a sequence of

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pictures, which shows an overview of the development of a human from fertilisation, into embryo, then foetus and child. Some of those pictures are photographs and some are ultrasound images. See also the discussion under Parturition, where we express the expectation that parturition management will be actually revolutionized by the introduction of the Ovulona into the obgyn practice.

Gonadotropins:

The hormones secreted by the pituitary gland of the brain that stimulate the function of the ovaries and testes (the gonads) to produce the gametes and the sex steroid hormones. They include the mentioned FSH and LH. The word gonadotropin is derived from the Greek gonad (an animal organ producing gametes = eggs and sperm; from Greek gonos for procreation or seed) and the Greek tropic for affecting or attracted to something specified, as in gonadotropic.

Gonads:

The organs that produce reproductive cells — the ovaries of women, the testes of men.

Gonorrhea:

A sexually transmitted bacterium that can cause sterility, arthritis, and heart problems [Greek gonorrhoia, flow of seed (from the mistaken belief that the discharge contained semen): gono, from gonos, seed, procreation + -rhoia, -rrhea, flow.]

Gynecology:

Sexual and reproductive healthcare for women. [From Greek gynh, gynaiko, a woman or female + -logy, from Greek –logia, science; theory; study (from logos, word, speech.] We note that a related word is gynaeolatry, meaning the adoration or worship of woman.

H

Hormone:

A chemical substance produced in one organ and carried by the blood to another organ where it exerts an effect. An example is FSH (follicle stimulating hormone), which is produced in the pituitary gland of the brain and travels via the blood circulation to the ovary, where it stimulates the growth and maturation of follicles. Hormones are naturally occurring substances with specific effects on physiological activities. Hormones are also involved in the complicated interactions between the different aspects of the organism that has resulted in the discipline called psychoneuroimmunoendocrinology, which directly applies to women's health issues, and which may be thought of as the scientific underpinnings of holistic medicine. In brief, chemical contraception uses synthetic steroid (ovarian) hormone analogs to suppress the production of one or both of the brain gonadotropic hormones (FSH and LH), which interferes with the normal regulation of the menstrual cycle. For more on how hormones work, see http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/moaction/change.html . For a better appreciation of the hormone phenomenon, please see Steroid hormone, below.

Hormone replacement therapy (HRT):

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The use of synthetic hormones, particularly estrogen, to replace the menopausal woman's diminished naturally self-generated supply of hormones. Prescribed to alleviate menopausal symptoms such as hot flushes, as well as to prevent osteoporosis. Menopause and HRT – initially as "estrogen replacement" or unopposed estrogen – did not come into vogue as a topic of concern for the medical profession until the 1960s, when chemical contraception was introduced. It is interesting to note that in countries in Asia and South America, where women eat either wild yams or soybeans, which are sources of progesterone, the term "hot flush" does not even exist in their languages. They also rarely suffer from the host of female problems presently plaguing Western women.

It is a fact that an estimated 40 to 50 million American women are now 50, the approximate average age of menopause onset. We believe that the Ovulona will be useful in menopause management in general, and personalization of HRT in particular. The latter has to do with the minimization of side effects of HRT. With respect to that, note that the risk of developing breast cancer, particularly the lobular subtype, is elevated with 'recent long-term' use of hormone replacement therapy, according to a report published in the February 2002 issue of the Journal of the American Medical Association. For more details, see Reuters Health Information 2002 at http://www.medscape.com/viewarticle/425187 .

HOT FLUSHES (OR FLASHES):

During the menopausal years, many women experience severe multiple symptoms, to a greater or lesser extent, depending on the individual. In fact, 70% of women experience hot flushes within 3 months of a natural or a surgical menopause. With some, the menopausal impact of estrogen deprivation can go unnoticed. The hot flush – or, medically, the vasomotor flush – is viewed as the hallmark of the female climacteric, experienced to some degree by most menopausal women.

The term is descriptive of a sudden reddening of the skin on the head, neck and chest, which is accompanied by a feeling of intense body heat and often by profuse perspiration. The duration varies from a few seconds (about 30) to several minutes, and rarely an hour or so. The episode ends usually in profuse sweating and a cold sensation. The hot flush frequency may be from rare to recurrent every few minutes, and the flushes are more pronounced at night or during times of stress. The disturbance of sleep results in fatigue, which may in turn lead to irritability, poor concentration, impaired memory, and other deterioration of quality of life. The vasomotor flushes are less frequent and less intense in a cool environment such as in winter months in the northern hemisphere. They can occur in pre-menopause, and are a major feature of post-menopause, lasting in most women for one or two years, but in as many as 25 – 50% of women for longer than 5 years. Unlike other aspects of menopause, hot flushes lessen in frequency and intensity with advancing age.

The physiology of the hot flush is still not well understood, but it apparently originates in the hypothalamus (in the brain) and is brought about by the decline in estrogen at menopause. Vasomotor flushes appear to result from a sudden lowering of the hypothalamic thermoregulatory set point. Activation of cutaneous vasodilation (increased blood flow into skin vasculature) causes an increased peripheral blood flow and thus heat loss, leading to a fall in core temperature. There are hormonal consequences as follows: About 3 to 6 minutes after the flush onset, epinephrine increases in blood (but not norepinephrine), and corticotropin acutely rises 5 minutes after the flush onset, leading to increases in cortisol (15 minutes), androstenedione (15 minutes) and dehydroepiandrosterone, DHEA (20 minutes). While luteinizing hormone (LH) increases and peaks about 12 minutes after the onset, growth hormone also rises, about 30 minutes after the flush. On the other hand, estrogen levels, as well as prolactin, FSH and TSH (follicle-stimulating and thyroid-stimulating hormones) remain stable during hot flushes.

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The flush may be preceded by palpitations or headache, and is often accompanied by weakness, faintness, or vertigo. It is understood in gynecology that 10 to 25% of women report hot flushes before menopause, and that women are often treated unnecessarily with estrogen for this relatively common psychosomatic symptom. In brief, the flush is not a release of accumulated body heat but is a sudden inappropriate excitation of heat release mechanisms. Its relationship to the LH surge and temperature change within the brain is not well understood. It is understood that the flushes are a consequence of the withdrawal of estrogens, rather than of hypoestrogenism (low estrogen levels) per se. The discontinuation of administered estrogens may also precipitate hot flushes, which may also be caused by the infertility drug clomiphene citrate (a nonsteroidal inhibitor of estrogen receptors in the brain). Obese women tend to be less troubled by hot flushes (because they are less hypoestrogenic).

An estimated 40 to 50 million American women are now 50, the approximate average age of menopause onset, and so it is not surprising that there is much discussion about whether hormone replacement therapy (HRT, see above) causes breast cancer or whether natural hormone creams are effective. The average woman experiencing the onset of menopause can get lost in all the controversies -- especially if she is already losing her normal composure because of distressing hot flushes and night sweats.

The bioZhena technology is expected to become a useful tool for the management of menopause, and specifically for the individualization of HRT or for the monitoring of the effects of any approach to menopause management. The concept of individualization of HRT has to do with the adjustment of hormone dosages, so as to minimize the drugs' harmful side effects. Alternative approaches include various uses of plant products with natural estrogenic and anti-estrogenic effects that balance and augment the body's hormone levels. For example, in The Hot Flash Cookbook (Chronicle Books, 1997), author Cathy Luchetti shares her thoroughly researched and tested nutritional solutions for relief of menopausal symptoms. In "No More Hot Flashes!" (http://216.205.123.2/whatshot/whatshot45.shtml), Luchetti is quoted saying, "I couldn't accept the very idea of HRT. I have never believed in pill-popping or other synthetic approaches to health. Yet, I had to do something, because I felt as if my once-dependable body and upbeat attitude were being chiseled away, bit by bit. And being a historian, I kept recalling all the Victorian stories of menopause that ended with the woman becoming 'unhinged by the change of life.' I refused to accept that as my fate."

Luchetti's words may be considered symptomatic of the attitude of many women today, and bioZhena is in tune with these changing attitudes. Unfortunately for some, though, with addiction and consumerism being what they are, some of our "thoroughly modern Millies" (pun intended) find it almost impossible to recognize that "…to try for hot-flash relief, you should avoid certain foods if you can -- especially spicy foods, caffeine, and sweets. Drinking alcohol can also trigger hot flashes". For those, there exist some over-the-counter herbal supplements "for ridding oneself of hot flashes and other menopausal symptoms".

As an objective and quantitative monitor of the effects of endogeneous or exogeneous (own-body-generated versus administered) steroid hormones, the bioZhena technology is expected to be a meaningful tool for menopause management, both in the hands of health providers as well as conceivably in the hands of the end-users themselves. This is a logical expectation because some women, especially those still having menstrual cycles, have apparently found that nutritional supplements (such as Dong Quai or Licorice Root) actually aggravated their symptoms. The proponents of these supplements argue that some of the herbs "don't agree with every woman" and that it is necessary to "give it time and carefully observe its effects in your body." As in any other situation, a good diagnostic tool is an advisable proposition.

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Hypothalamus:

A small part of the brain located just above the pituitary gland. It regulates basic animal functions, and is involved in the regulation of the menstrual cycle including the timing of ovulation. It produces pulses of the GnRH (gonadotropin releasing hormone), a hormone which stimulates the pituitary gland to produce and release the gonadotropins FSH and LH, the brain hormones that lead to follicular development and ovulation. The hypothalamus acts as a computer, analysing nerve signals from other areas of the brain including those generated by emotions, and by environmental factors such as stress and nutrition. It also analyses hormonal signals (estrogen and progesterone) generated by the ovaries and other endocrine glands. The sum total of these effects determines the quality of the ovarian activity, that is when or even whether ovulation will occur. Hypothalamic dysfunction, involving a malfunctioning GnRH pulse generator, leads to anovulation and amenorrhea (see above).

I

Implantation:

The attachment of the pre-embryo to the lining of the uterus.

Infertile phases:

The phases of the menstrual cycle (or of the estrous cycle in animals) when pregnancy cannot occur. There is a preovulatory and a postovulatory infertile phase, which together constitute the large majority of the reproductive cycle.

Infertility:

Clinical infertility is the inability of a couple to achieve a pregnancy or to carry a pregnancy to term after one year of unprotected intercourse. If the difficulty to conceive lasts less than a year, the condition is referred to as reduced fertility or sub-fertility. Clinical infertility is classified further into male infertility, female infertility, couple infertility, and unexplained infertility. Studies have shown that in the past 50 years the quality and quantity of sperm has dropped by 42% and 50% respectively. In the past 20 years the decrease in sperm counts has occurred at a rate of 2% annually. For further information refer to Xeno-estrogens (below) and the web reference therein. In the U.S. alone, of the 6.7 million women with fertility problems in 1995, 42% had received some form of infertility services. The most common services were advice and diagnostic tests, medical help to prevent miscarriage, and drugs to induce ovulation [Fam. Plann. Perspect. 2000 May-Jun;32(3):132-7].

A Glossary of Infertility Terms and Acronyms published by the InterNational Council on Infertility Information Dissemination is available at http://www.inciid.org/glossary.html .

IUD (intrauterine device):

A small device made of plastic, which may contain copper or a hormone, that is inserted into the uterus by a clinician. A reversible method of birth control available only by prescription.

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L

LH or luteinizing hormone:

A hormone released by the pituitary gland in the brain to signal the initiation of ovulation. Basically, the brain signals to the ovary to change the selected or dominant follicle into a luteinized yellow "body" or corpus luteum.

Luteal phase:

The postovulatory phase of the menstrual cycle, from ovulation to the onset of the next menstruation. It typically lasts 13 or 14 days, although some authors put the range at 12 to 16, but the luteal phase usually does not vary more than 1 or 2 days within individual women. That relative constancy differentiates the luteal phase from the highly variable pre-ovulation phase (called the follicular phase).

Luteinized unruptured follicle syndrome or LUFS:

A condition in which the ovum remains stuck within the luteinized follicle, unable to pass through the ovarian wall to a possible conception. It is now believed to be a major cause of unexplained infertility.

M

Mammary:

Of or relating to the milk-giving gland of the female. For optimal milk production, dairy farmers need to get their cows pregnant again (re-bred) at the right time, otherwise they lose money. Determination of the optimal breeding time is the purpose of the agricultural application of the BioSense technology.

Mammogram:

X-ray photographs of the breasts that can detect cancerous tumors before they can be felt.

Menopause:

The time at "midlife" when menstruation stops; a woman's last period. This happens when the woman's stock of eggs in her ovaries has become exhausted. It usually occurs between the ages of 45 and 55. "Surgical menopause", however, which results from removal of the ovaries, may be caused to occur earlier. It is interesting to note that menopause (and hormone replacement therapy) did not come into vogue as a topic of concern for the medical profession until the 1960s, coincident with the development of oral contraceptives. The bioZhena technology may be expected to become a useful tool for the management of menopause, and specifically for the individualization of HRT (hormone replacement therapy, see above) or for the monitoring of the effects of any approach to menopause management. The concept of individualization of HRT has to do with the adjustment of hormone dosages, so as to minimize the drugs' harmful side effects. See also under Hot flushes (or flashes), under Osteoporosis, and under Atrophy. More on menopause and HRT in the entry below.

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MENOPAUSE, HRT, AND BIOZHENA:

The author of the highly recommended book "Woman - An Intimate Geography" made a serious mistake in her take on her "miraculous" conception, assuming that it occurred outside of the fertile period (see under Mysterious conceptions, below). But Ms. Angier has not been awarded the Pulitzer for the color of her eyes – and her book is a marvelous companion read for the bioZhena project. Thus, follow her narrative on menopause and HRT…
… and see why this – menopause and HRT - is such an enormous opportunity for bioZhena.

Incomparably bigger than, for example, early detection of cervical cancer (13,000 cases diagnosed annually, resulting in 4,100 deaths), although that, too, is a worthwhile target, particularly in terms of public health in developing countries. For "here we are, saddled with another gynecrisis, …, this crisis perhaps the biggest one ever… about 50 million women in the United States over the age of fifty, all of them potential candidates for hormone therapy. If every one of them were to take hormone pills for the next thirty years … that amounts to 1.5 billion woman-years of drug consumption. What an absurdly huge number. Never before has a drug regimen been proposed on such a scale. Can we expect unity and revelation from the teeming ranks of womankind? Can we expect a simple yes-or-no answer to the question 'Should I take hormone replacement therapy?' "

Ms. Angier gives an excellent explanation of why there is no simple answer (because "hormones have much to offer, but still they smirk ever so slightly. They are a little dangerous, a little threatening. … We live in the age of mindful menopause, forced to dwell on the change and its aftermath as our foremothers never did"). A number of studies have shown that the risks of contracting breast cancer increase the longer a woman takes estrogen replacement therapy. Ms. Angier highlights the situation with the so-called designer estrogens that pharmaceutical companies are racing to develop ("which in theory will offer the benefit of tissue specificity, of protecting the parts that need protecting while ignoring the tissues, like the breast, that don't want the stimulus…"). We pinpoint a few bits from her narrative, leading to the conclusion that a diagnostic tool for patient management is of great importance in this situation – to help the women, the medical profession, and the pharmaceutical industry that drives the opinions of the other two.

"Most gynecologists and internists today think that hormones are the right choice for most menopausal women. Yet, they concur that the therapy is not without risks… Women must decide for themselves… We love estrogen, and we fear estrogen. Everybody wants to take it. Why do so few women take it? We can't be blamed for our volatility. The scientific literature is volatile, and it is vast. We are chased and torn… There is no escaping the drone of menopause consciousness… menopause has exposed itself to homily, reductionism, and medical sharecropping. You say middle-aged woman, they say HRT…"

"Over the past few years, the medical juggernaut in favor of hormone therapy has barreled ahead with spectacular determination… What a vociferous, clanking tank the medical consensus can be. It has so much work to do, so many millions of women to persuade… Whenever a new study comes out suggesting an increased risk from hormone therapy of breast cancer, uterine cancer, or ovarian cancer, defenders of the universal solution storm in to put the result 'in perspective'. [They storm in] to remind us that heart disease, not cancer, is the biggest killer of women, and that the risk of osteoporosis is greater for a woman than her risk of breast, ovarian, and uterine cancer combined." [Homily, a sermon, especially one intended to edify a congregation on a practical matter and not intended to be a theological discourse; a tedious moralizing lecture or admonition. Sharecropping by definition is the working of a piece of land by a tenant in exchange for a portion, usually half, of the crops or the revenue that they bring in for the landowner. Sharecropping appeared in the Southeastern

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United States, including Appalachia, after the Civil War as a way to continue post-slavery white supremacy over African Americans, but it ultimately included poor whites as well.]

In chapter 12, Ms. Angier further explains (on page 210) that "considered broadly, hormone therapy 'works' – that is, it reduces mortality by a fairly impressive margin… For example, the women on hormones had a 40 percent lower risk of dying during a given year than women who had never taken hormones, mostly as a result of a decline in heart disease. That's the big picture…" Let the Pulitzer writer speak further on the subject. "Of course, there is more to life than dodging death. Hormone therapy can improve the tone of life. It inhibits the dissolution of bone, that gradual regression to the bog collective. Women who take hormones have a 50 percent lower risk of fracturing a hip than non-compliers… Hip fractures are the primary reason that people over seventy end up in nursing homes. Hormone therapy… helps prevent incontinence, and it prevents the vaginal wall from getting thin and dry… The performance of the urogenital tract is no small matter on the quality of life front. And then we have the brain, our beloved brain. Several studies indicated that estrogen therapy may reduce the risk of Alzheimer's disease by about 50 percent. Many women who take estrogen replacement therapy like how they feel on the drug. They find that estrogen helps stabilize their mood and that it improves their memory."

Here is a significant quote from page 212, highlighting a key socio-economic aspect of this "designer – therapy", the new phenomenon of our era. "Complain though American doctors will about the low compliance rate of their postmenopausal patients, American women lead the world in the use of hormone therapy, just as they do in the rate of hysterectomies. In the United States, 46 percent of postmenopausal women take or have taken hormone therapy. British, Australian, and Scandinavian women come next, with ever-used rates of around 30 percent. Continental Europeans are notably less enthusiastic about medication…"
And now for the key phrase, emphasizing the need for individualization of HRT: "We also know that hormone therapy has risks as well as benefits, and that there's no escaping the complexity of the body or the individuality of any one body and its history. We are back where we began, forced to decide case by case…"

The Ovulona is an individual woman's health monitoring tool, primarily responsive to her steroid hormone profile. As such, it may be expected to become useful for the management of menopause, and specifically for the individualization of HRT (hormone replacement therapy, see above) or for the monitoring of the effects of any alternative approach to menopause management. The concept of individualization of HRT has to do with the adjustment of hormone dosages, so as to minimize the drugs' harmful side effects. The bioZhena technology is an objective and quantitative monitor of the effects of steroid hormones - whether endogeneous or exogeneous (own-body-generated versus administered). On this basis, it is expected to be a meaningful tool for menopause management, both in the hands of health providers as well as conceivably in the hands of the end-users themselves. Besides causing the Ovulona to become a widely used personal tool for women's health management in the reproductive years, there is a good chance that the technology will naturally extend its usefulness into the post-reproductive years.

Menstrual cycle:

The time from the first day of one menstrual period to the first day of the next period. The cycle is a repeating pattern of fertility and infertility. The menstrual period involves cyclical changes in the ovaries, cervix, endometrium, and in the brain, under the control of the sex hormones (LH, FSH, estrogen and progesterone). Most of the time within the menstrual cycle, the female is infertile; the fertile window, during which conception can occur, is quite narrow (see under Fertile phase or fertile window, and under Fertility, above).

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Menstruation:

The cyclical occurrence of a flow of blood, fluid, and tissue out of the uterus and through the vagina that usually lasts from three to five days. The first day of menstrual flow is both the last day of the current menstrual cycle and the first day of the next cycle. Menstruation occurs when the ovulated egg has not become fertilized, that is when conception has not occurred.

Method effectiveness:

The reliability of a contraceptive method itself — when it is always used consistently and correctly. The reliability of different methods is also compared in terms of method failure. This is what the independent non-profit Allan Guttmacher Institute has to say: "Some of the failure is due to the methods themselves, but most is a result of the difficulties that individual women confront in incorporating the task of contraceptive use into their everyday lives; over half of all women practicing contraception use a method that requires ongoing attention (as opposed to surgical sterilization). They include women who rely on oral contraceptives as well as those using intercourse-related methods such as the condom and the diaphragm. Practicing the prevention of pregnancy, therefore, is at least as difficult as other such preventive health strategies as maintaining a proper diet, exercising and quitting smoking." Natural family planning research has shown that among the advantages of the NFP practice is that the inherent discipline enhances the sexual relationship and dialogue, which leads to high levels of satisfaction. Citation reference: http://www.alanguttmacherinstitute.org/pubs/ib19.html

Modus operandi:

Abbreviated MO. A method of operating or functioning, a manner of working. [From New Latin modus operandi: Latin modus, mode + Latin operandi, genitive sing. gerund of operari, to work.] It is a safe bet that this phrase would be found (http://www.amazon.com/exec/obidos/ASIN/0395893380/lexico) in The Big Book of Beastly Mispronunciations as "modas operandai", because of the popularity of the expression, which in science and medicine becomes – for a change! - the plain "mode of action". Any system or process has its MO, of course, as in …Predatory Pricing - Microsoft's Modus Operandi, by William C. Spaulding: How Microsoft uses predatory pricing to establish its monopolies... Category: Society > Issues > Economic > Monopolies and Oligopolies > Microsoft > Against money.york.pa.us/Articles/Microsoft.htm .

Please note that, while it is intended to make this an easy read, below you will be asked to concentrate and take in the idea being disclosed. On the surface, the mode of action of the bioZhena technology is quite simple at its sensor "business end", which – along with the elegant smallness of the personal product – makes for "beautiful in its simplicity". Furthermore, we insist that the product concept is decidedly customer-friendly, not only in the appearance but also in the user interface and software aspects. Thus, we are talking about the antithesis of your TV/VCR remote control! Whether we are referring to the Ovulona or to the veterinary BioMeter, and whoever is the intended end-user, this is not an engineer's tool but an easy consumer product.

The mode of operation of the underlying technology is called admittance measurement, and it is designed to be absolutely innocuous to the object of measurement. This feature is fundamentally different from the MO of the so-called prior art devices of the vaginal kind that are to be found in the patent literature. Innocuous is an adjective that means having no adverse effect; harmless, and also not likely to offend or to provoke strong emotion. Actually, the latter is in the absolute only true in the case of women, as opposed to the males, who tend to lack the basic or inherent appreciation of the apparent MO of the technology, which of

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course involves a thoroughly gender-specific aspect of female anatomy and physiology. [From Latin innocuous: in-, not + nocuus, harmful, hurtful, from nocere, to harm, to hurt].

There is on the market another vaginal probe, superficially somewhat similar to ours (although it requires another, oral, probe to be of any use), and a few others have been described in the patent literature. They are all about the measurement of conductivity of the vaginal fluids. Invariably, the vaginal probes of other inventors expose their female subjects to large electric currents, and to the harmful effects of the accompanying electrolysis of the tissues and body fluids in contact with (or adjacent to) their electrodes.

As a prospective participant with bioZhena, the reader is presumably interested in the prior art aspect of the project, and wants to appreciate the distinguishing features of the bioZhena technique and products. Unlike some of the prior art, this technology development started with the human application before being extended into the animal domain. As the original purpose of the effort was the very personal need to assist conception, the primary criterion of design was "first and foremost, do no harm" – to the prospective Mum and partner. This is why we control the potential, applied to the electrodes and kept at miniscule levels, incapable of causing electrolysis. With the sufficiently high frequency of the excitation waveform, we tap into the capacitive response of the tissues in contact with the electrodes, avoiding any faradaic currents from occurring. The opposite is true of the so-called prior art devices, which pass extremely high currents, inevitably electrolyzing the vaginas, and releasing into them harmful metal ions. Such foreign metal ions – as a matter of principle - modify the biochemistry of the vaginal tissues, to the detriment of the subjects of measurement.

The bioZhena technology, which has been optimized for use in the given mammalian species, also avoids by design the reliance on any reference electrode, again for safety reasons as well as for reasons of practicality. Finally, the bioZhena technology taps into the physiology of the cervical tissues that we have discovered as an intrinsic monitor of the so-called hypothalamic-pituitary-ovarian axis (HPO axis). The HPO axis is the regulatory (feedback) system that governs menstrual cycles, and includes the brain and the reproductive tract. For more on this, see under Axis, above.

Here now comes one of the two or three places in the Alphabet of bioZhena, where you are asked to concentrate and take in the idea being shared with you. (The other such appear in the third paragraph of the entry on Sexually Transmitted Diseases, and in the entries on Cervical cancer, and on Smoking. Ultrasound scanning might well be mentioned here, too.)

The core bioZhena devices' mode of action is controlled-potential, and controlled-location, admittance measurement. This is very different from the high-current vaginal-fluid impedance measurements of other people's conductometric techniques. Herein lies the crux of the matter. Where the superficially possibly similar (similarity being in the eye of the beholder) prior art registers the maximal admittance due to the temporarily elevated electrolyte and water content around ovulation, the bioZhena sensor registers precisely the opposite, the lowest admittance of the menstrual cycle, indicative of ovulation in the human female. And vice versa, our highest admittance signal is obtained early in the cycle, during the so-called dry days. During the dry days, when there is little, if any, vaginal fluid to be observed, the conductometric prior art logically registers high resistive impedance, that is low admittance. Other people's vaginal conductivity measurement cannot reflect the dominant follicle maturation (because it is not reflected in the electrolytes of the body fluids). Only our tissue-biosensor transducer can register the inputs that the given tissue receives from the HPO axis.

Where other devices probe for conductivity changes of the vaginal fluids, our sensor may – to some - look superficially similar, but it does something completely different. That is why our cyclic profile has such high information content whereas the conductometric curves are

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basically flat (devoid of information) on both sides of their single, electrolyte-driven, mid-cycle inflection. Only the Ovulona provides not only a short-term anticipation of ovulation but also an earlier long-term predictive signal. This long-term predictive peak really has no counterpart among the various other methods of fertility monitoring. Its position ahead of ovulation apparently depends on the rate of maturation of the dominant follicle in the given menstrual cycle, and it correlates with (and generally determines) the length of the menstrual cycle.

Two other important features distinguish the bioZhena technology from the putative competitors: One, the conductometric probes yield different range of response in different individuals, whereas our dynamic range is the same within the given species of mammals (e.g., in different women). And two, unlike the conductometers of prior art, our technology exhibits species differences, including the tracing of the single dominant follicle maturation in the human female versus the follicular waves in livestock.

In this context, the reader is reminded that only our tissue-biosensor technology can respond to a variety of physiological events beyond the straightforward menstrual cycling. Based on the discussed MO, we are encouraged by our data to date. These happen to include an aberrant cycle devoid of the dominant follicle maturation signature, and correlated with BBT data that are consistent with luteal phase defect (although this requires further investigation, and could be a different type of abnormality frequently seen in healthy young women). We are optimistic about finding distinct signatures for different aberrations involving the cervix (directly or even indirectly, through the HPO axis). The monitors of body fluid ionic conductivity or hormone content simply cannot do this, as a matter of principle.

We conclude this summary of the mode of action by emphasizing the importance of our technique's marker of ovulation, which is separate from the predictive signals, and only available here, as opposed to the competition methods of any kind (vaginal or oral probes, or urinary hormone testers). In the other methods, ovulation is not detected but merely assumed to occur so many hours after detecting a predictive hormone-driven signal.

As the expert, Professor Kamran Moghissi, M.D. (http://obg.med.wayne.edu/Department/Faculty/moghissi.htm), used to caution his gynecological colleagues some years ago, most of those twenty-plus measurable parameters associated with the menstrual cycle reflect the underlying hormonal changes but not the ovulation event as such. Only our end-organ monitor of folliculogenesis can do that. See also under the Ovulona, below. See also under Mysterious conceptions (or the lack of thereof). An example of Professor Moghissi's work is: Kamran S. Moghissi, "Cervical mucus changes and ovulation prediction and detection", Journal of Reproductive Medicine, Volume 31 (No.8), Supplement, 748 - 753, 1986. In a discussion, captured on page 771, Dr. Moghissi has this to say [QUOTE]: I believe there are variations from cycle to cycle for a normal woman, as illustrated in an infertility patient who has a double uterus and cervix and a single vagina. In doing postcoital tests, we found that the number of sperm per high-power field was very different. One cervix produced copious mucus, the other very little. This shows the variation in target tissues in the same individual [END OF QUOTE]. We cite this, of course, to drive home the concept of end-organ effects and tissue biosensor as the approach to fertility monitoring.

"Morning-after" Pill:

Emergency hormonal contraception that is taken within 72 hours of unprotected intercourse. See under Emergency contraception.

Mysterious conceptions (OR THE NONEXISTENCE THEREOF):

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It appears that we must dwell on this topic, because of stories and notions propagated in various pertinent circles. This writing has been prompted by page 176 in the excellent 1999 book "Woman" by Nathalie Angier, where the Pulitzer laureate relates the story of the mysterious conception of her only child. Mysterious, because it occurred, she believes and makes her readers believe, outside of ovulation and of the fertile window. The reason for this entry in the Alphabet of bioZhena is that there is **NO SUCH THING AS MYSTERIOUS CONCEPTIONS**, there is only lack of information, or ignorance of the facts. We might say, intellectual misconceptions lead to "mysteries" in terms of conception, of babies conceived supposedly when conception was biologically impossible, and vice versa, some women have difficulties conceiving for the same fundamental reason. We shall use Ms. Angier's case to make this point.

Ms. Angier admits that she has "been seduced by experience, my personal encounter with the fertility spirits. My husband and I had been trying for years to become pregnant. I cycled like a metronome, every twenty-eight days. And for a while our sex became metronomic too, concentrated furiously around midmonth, when I thought I was likeliest to conceive. … I used ovulation predictor kits to detect my LH surge. For months, we abided by the thin blue line. Nothing happened, nothing, nothing, nothing."

"In November of 1995, my little predictor sticks failed to detect evidence of an LH surge. I was terribly glum about that: an anovulatory cycle, I thought, and there I was, thirty-seven years old, running out of time. But in December I found out I was pregnant – that I had conceived the month before, when I was certain all lay fallow. I reviewed the sequence of events, and I knew what had happened. Early in my cycle, days before I thought conception was possible, my husband and I had done what we managed so rarely in those times of procreation fixation and had sex for the pure love and pleasure of it. That act, I am sure, that pointless, magic squander, pumped up my cycle… My climax quickened the hatching of an avid egg. It provoked an LH surge, and the surge spurred a follicle, and the egg broke free and dove down a tube, and the sperm from the precipitating event was there to greet it. And everything fell into place so swiftly that by the time I started the usual midmonth screening for an LH surge, I had missed the excitement. I thought I lay fallow, but in truth I already was in clover. I have no proof of any of this, of course. All I have is my child…"

Except that there is a perfectly rational explanation for the beautifully described experience (repeated, no doubt, in many homes the world over), quite apart from the fact that – unwittingly – Ms. Angier has also brought out the fundamental fallacy of the current popular technology tool, the LH kit. The fundamental problem with the LH kit is of the same kind as the misconception that Ms. Angier so skillfully helps to propagate. The Pulitzer-winning writer assumes that she "cycled like a metronome, every twenty-eight days", and the LH kits assume that a woman can estimate the limited period, during which to use those kits, from her prior experience of her menstrual cycles. Well, as we have said on numerous occasions, there is no such thing as predictability of the fertile window, just as there is no such thing as a workable "rhythm" method of birth control.

The perfectly rational explanation of Ms. Angier's experience is that, contrary to her belief of having absolutely regular cycles (of 28 days at that, what a magical coincidence with the textbook "standard 28 day cycle"!), she just cannot be that regular, because nobody is. How do we know? Easy. In the years when the thermometer was the only available tech tool for fertility awareness, and there was the hope that the BBT would solve all the reproduction management problems, many studies were conducted in support of that expectation. Here is a summary of the outcome of those studies:

Rather than result in a reliable fertility monitor, the many published basal body temperature studies have demonstrated that menstrual cycle regularity is a myth. Most women experience

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changes of more than five days in the length of the menstrual cycle. Less than 1% of women would be found with no variation at all, even for short sequences of only a few menstrual cycles [3]. Two longitudinal studies are probably the most frequently cited sources of data on this subject, published by Vollman [4] and by Troelar et al. [5]. The cited references and further details will be found in the white paper "The BioMeter: An in vivo tissue biosensor for fertility awareness and possible additional applications. Part 1. A review of the fertile window problem, and of the commercially available technologies addressing the problem". See section "A critical review of commercially available fertility diagnosis technologies", at http://biosense.freeservers.com/custom2.html .

To drive the point home, here is an excerpt from the paper cited above as reference [3], which is: John J. McCarthy, Jr. and H.E. Rockette, "Prediction of ovulation with basal body temperature", Journal of Reproductive Medicine, Volume 31 (No.8), Supplement, 742 - 747, 1986. The BBT experts have this to say [QUOTE]:

Cycle regularity is often assumed by both women and their physicians. The suggestion, that the BBT graph of the previous cycle can be used to identify the day of ovulation in the current cycle, requires nearly absolute cycle regularity. The data collected by 1,085 women, who provided at least 6 or more charts [each], were studied for cycle length variability. … The cycle length range was more than five days for 56% of the women who submitted 6 graphs, and for 75% of those with 12 graphs. … Absolute regularity was not demonstrated in as few as six cycles. Even when the cycle length that deviated [the] most was eliminated, less than 1% (8 of 1,085 women) had no variation in cycle length. When the number of cycles was extended to 12, no woman had variability of less than two days in cycle length [END OF QUOTE].

In real life, of course, no cycle can be eliminated from the experience, and every day matters. This is therefore the basis on which we can say quite categorically that nobody is as regular as a metronome (and nobody conceives in an anovulatory cycle), that there is no such thing as absolute regularity, whether 28 days or otherwise.

For example, in the Marquette University pilot study of an early prototype of the BioMeter/Ovulona technology, the cycle lengths ranged from 23 to 35 days in a group of 21 cycles recorded by 10 women. The estimated timing of ovulation ranged from day 9 to day 23 (or from day 10 to day 24, depending on the method of detection: LH kit, peak mucus, and BioMeter prototype). Only 2 of the 10 women appeared to possibly ovulate on the same day of cycle in two successive menstrual cycles (but only by the peak mucus and the LH kit data -- not by the data yielded by the BioMeter prototype).

Such an outcome is quite consistent with the results of large clinical studies including those focused on cycle length investigation: [3], [4], [5]. The one subject in the Marquette pilot study who monitored four successive menstrual cycles, a 41 year-old nulliparous woman [with no children], produced the following data for the estimate of the ovulation day in the successive four cycles:

14, 13, 15, 14 by LH kit,
15, 14, 16, 13 by peak mucus, and
18, 13, 18, 15 by BioMeter prototype.

The discrepancies among the methods are as expected, as is the spread of the ovulation-day data. The LH kit and peak mucus methods are no "gold standard" methods for the detection of ovulation; they are merely hormone-based tools for its estimation (see respective entries, above and below, for details). The BioMeter data can be seen as illustrating delayed ovulation in the first, third and the fourth cycles, an illustration of the importance of detecting ovulation independently of ovulation prediction.

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Usually, ovulation occurs within hours of the LH peak, and approximately on the day of the peak mucus. Only the BioMeter (a.k.a. Ovulona) can detect the important deviations from this estimation. Every day can make the difference between conception and the lack thereof. As for the reason for the illustrated variability, Natalie Angier puts it very nicely on page 168 [QUOTE]: The ovulatory cycle is a matter of physiology, and it occurs more or less on its own. But it is not entirely deaf to the cyclist. We don't want to make the mistake of thinking it is disembodied from the body. To the contrary, … the first half of the cycle is the most impressionable time. Women have very different cycle lengths, some as short as three weeks, others as long as forty days, and most of that variability occurs in the days between menstruation and ovulation. After the egg is released, the cycle becomes much more predictable. It lasts two weeks, give or take a couple of days. [We would add, "in many cycles but not in all, by any means". However:] Before ovulation, the ovary is like an appellate court. It will listen to pleas and hear tales of denial and doubt. It will take advice of a number of signals – from the brain, surrounding tissues, distal tissues – about what to do, whether to ovulate or vegetate. … Whatever the details, it is not a bad system [END OF QUOTE]. Indeed, it is not a bad system; it makes the BioMeter (or Ovulona) technology possible!

Returning to Ms. Angier's story of mysterious conception, it is one thing when a popular science writer exercises her poetic license (about the fertility spirits, and a magic squander pumping up her cycle…), which will unfortunately influence the thinking of her readers. But, there are also too many sources of such mistaken notions in the specialist circles, among those who "should know better". We aim to do something about that, of course.

N

Natural family planning (NFP):

Refers to several different methods for spacing, postponing, avoiding or enhancing the possibilities of conception, without any chemical or physiological alterations of the reproductive system (female or male). Natural family planning research has shown that among the advantages of the NFP practice is that the required discipline enhances the sexual relationship and dialogue, and that there is a reduction of "dominant attitude" in both men and women practising NFP. Contemporary methods are sometimes referred to as 'fertility awareness' (FA) since they are ultimately based on awareness of symptoms of fertility that are readily recognizable or measurable by any woman. Other people distinguish between NFP and FA in terms of the fertile phase: NFP users abstain whereas FA users employ a barrier method of contraception. In any case, NFP and FA are distinct from the older 'calendar' methods such as Ogino-Knaus (the so-called 'rhythm' method).

The American College of Obstetricians and Gynecologists refers to "family planning by periodic abstinence" and explains that this is [QUOTE] another name for the method of birth control that used to be called 'rhythm method' or 'safe period'. More recently it has also been called 'natural family planning' or 'fertility awareness'. It isn't a single method but a variety of methods. Each is designed to help a couple find out which days during a woman's menstrual cycle she is likely to be fertile or able to become pregnant [END OF QUOTE]. For the citation, see Sperm and semen, below. While the proponents of NFP warn that, without further expenditures on education, NFP will remain a fringe method in the U.S., the American College of Obstetricians and Gynecologists advises the public that [QUOTE] periodic abstinence is quite an effective means to prevent an unwanted pregnancy [END OF QUOTE].

Norplant®:

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A contraceptive system of six small soft capsules containing the synthetic hormone levonorgestrel that is inserted under the skin of the upper arm. A reversible method of birth control that is available only by prescription.

O

Oocyte:

A cell from which an egg or ovum develops by meiosis; a female gametocyte that develops into an ovum after two meiotic divisions.

Oral contraceptive (OC):

The birth control pill. Also called the Pill. The Physician's Desk Reference carries the following warnings: The use of oral contraceptives is associated with increased risks of several serious conditions including myocardial infarction, thromboembolism, stroke, hepatic neoplasia, and gallbladder disease, although the risk of serious morbidity or mortality is very small in healthy women without underlying risk factors. The risk of morbidity and mortality increases significantly in the presence of other underlying risk factors such as hypertension, hyperlipidemias, hypercholesterolemia, obesity and diabetes. Cigarette smoking increases the risk of serious cardiovascular side effects from oral contraceptive use. This risk increases with age and with heavy smoking (15 or more cigarettes per day) and is quite marked in women over 35 years of age. For more about chemical contraception, see the Pill.

Meanwhile, one hundred women who claim they were seriously injured by third-generation oral contraceptives will seek "substantial damages" from manufacturers in a court case in Britain. Claims were being made against Organon Laboratories, Schering Health Care and Wyeth. The trial, starting on March 4, 2002 at the High Court in London, followed seven years of controversy over the safety of the third-generation pill. The claims date back to the 1995 'pill scare' which led thousands of British women to stop taking third-generation pills after studies reported an increased risk of blood clots.

If you have checked out the story of the Pill (below), you may have noted that one of the so-called Fathers of the Pill mused in the sense that if he could do it again, he would try and minimize the required intake of the contraceptive drug, ideally to a once-a-month inducer of menstruation. Well, they may not have it quite that way, but see this: "Mifepristone shows promise as oral contraceptive agent. Mifepristone, also known as the RU-486 pregnancy-terminating agent, can inhibit ovulation and induce amenorrhea. It could, therefore, represent a novel estrogen-free oral contraceptive agent, according to a recent report." At least, they have done away with the chronic administration of the xeno-estrogens and the progestin xeno-progesterones. Instead, this compound is used acutely, on an "as needed", "case by case", basis. For more details, view Reuters Health Information 2002 at http://www.medscape.com/viewarticle/425585 . The U.S. Department of Health and Human Services announced in September 2000 that the Food and Drug Administration has approved mifepristone for the termination of early pregnancy, defined as 49 days or less, counting from the beginning of the last menstrual period.

Do we need to debate whether it is preferable to do away with these xeno-steroids all together?

For any such debate, here is a fact of interest (http://darwin.bio.uci.edu/~sustain/bio65/lec07/b65lec07.htm) highlighting that medicinal

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compounds, although "xeno-", have been used even before the era of modern medicine. (Perhaps what matters the most is how… Occasional use is very different from chronic mass application, is it not.)

The Neem tree, in India, has been found to be a source of materials that prevent implantation or cause abortion. The Neem, sometimes called "the village pharmacy", is also a source of a spermicide, as well as of an insecticide, and of some fungicides, etc. The tree has been used in traditional medicine, agriculture, and cosmetics for centuries. Not surprisingly, some companies from Western countries have been seeking to exploit the tree, and 90 patents have been granted worldwide for "inventions" of products from the Neem. However, a coalition of organizations has been fighting patenting of materials already in traditional use ("bio-piracy"). In 2000, they persuaded the European Patent Office to (logically) revoke a patent from the USDA and W.R. Grace on a Neem tree fungicide - on the basis that the product was already being used traditionally in India, before the Grace Company patented it.

In fact, as in the story of the Pill (see below), numerous organic chemists have devised ways of synthesizing many of the medicinal compounds found in plants. It turns out that it is usually cheaper to extract the natural product. In spite of this, American pharmaceutical firms are, generally (with one or two exceptions), doing little to discover new drugs from higher plants, and are concentrating on other approaches; specifically, on using supercomputers to design new (hence patentable) molecules. Those are then imposed on the public by vigorous marketing (and their side-effects often controlled by other molecules, thus adding to the revenue stream…).

Osteoporosis:

A disease in which the bones become extremely porous, are subject to fracture, and heal slowly, occurring especially in women following menopause and often leading to curvature of the spine from vertebral collapse. [From New Latin osteo- from Greek osteon, bone + Greek poros, passage, pore + -osis, a suffix signifying a condition, process or action, often a diseased or abnormal condition.] The adjective form is osteoporotic. Osteoporosis is largely a disease of modern civilization. Bones are complex living tissues with many nutritional and hormonal needs. Failure to meet any of these needs compromises the strength and integrity of bone tissue. Diet and environmental conditions are apparently related to this modern epidemic.

Osteoporosis is epidemic in the United States, affecting more than 20 million individuals. The increase in osteoporotic fractures is actually a major global public health problem. It appears that women lose more bone today than they did some 200 years ago, perhaps due to less physical activity and other factors such as a dietary decrease in dairy products, and an earlier and greater loss of bone because of the impact of cigarette smoking.

Estrogen therapy has been found to stabilize the process of osteoporosis or prevent it from occurring. There is a critical blood level of estrogen (estradiol) that has been found necessary to maintain bone. However, protection against fracture wanes with age. The precise mechanism of action of sex steroid protection of bones remains unknown. While progestational agents are considered anti-estrogenic, they have been known to act independently, in a manner similar to estrogen, to reduce bone resorption. There has been considerable confusion over whether calcium supplementation by itself can offer protection against postmenopausal osteoporosis.

As in any other situation, a good diagnostic tool for the management of the problem is a desirable proposition, and our Ovulona is expected to become such a tool. Simply stated, this expectation is based on the fact that the response of the bioZhena technology is basically driven by steroid hormones, via the end-organ effect upon cervical tissues.

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Ovaries:

The two small, oval shaped, organs that store eggs in a woman's body from her birth until her menopause. [From New Latin ovarium, from Latin ovum, egg.] The ovaries also produce hormones, including estrogen, progesterone, and testosterone. The two almond sized ovaries are perched in the pelvis, one on each side, just within the fallopian tubes' grasp. Each month, at the time of ovulation, a mature egg is released by one ovary. This egg (or oocyte) is picked up by the bordering fringe at the end of the fallopian tubes (called the fimbriae), and drawn into the fallopian tube (oviduct).

It is an interesting feature of Nature's design that, although the ovaries are attached to the body of the uterus by a sort of a stalk, this physical connection is not utilized for the egg transport. That occurs in a roundabout manner, involving the release of the egg into the peritoneal cavity (in the belly) where it is promptly picked up by the blood-engorged fimbriae, as stated above. The finger-like fimbriae are brought into close contact with the surface of the ovulating ovary by the muscular activity of the mesotubarium (a fold of the peritoneum - the membrane that lines the walls of the abdominal cavity and encloses the viscera - which connects the ovary with the wall of the abdominal cavity).

Listen to this: "The ovary is moved slowly to and fro and around its longitudinal axis by contractions of the ligamentum ovarii proprium. The oocyte is engulfed into the infundibulum [the ovarian opening of the fallopian tube], and within minutes transported to the ampullary isthmic junction by segmental and peristaltic contractions of the oviductal musculature… The human isthmus and ampullary isthmic junction have a rich adrenergic plexus intermingled with the circular muscle fibres. In the ampulla, adrenergic nerve distribution is sparse… Thus, the isthmus probably functions as a physiologic, if not anatomical, adrenergic sphincter." [Hafez and Evans, editors, Human Reproduction: Conception and Contraception, Harper & Row, 1973, page 109]. A sphincter is a ring-like muscle that normally maintains constriction of a body passage or orifice and that relaxes as required by normal physiological functioning. See also Understanding cancer of the ovary at http://www.cancerbacup.org.uk/info/ovary.htm .

This is how Natalie Angier relates to the ovary in her remarkable book, "Woman": "The ovary is no beauty… a healthy ovary looks sickly and drained of blood… it is scarred and pitted, for each cycle of ovulation leaves behind a white blemish where an egg follicle has been emptied of its contents. … The ovary is gray because it alone among residents of the pelvic cavity is not covered by the pinkish peritoneum, the springy membrane that encloses and protects other organs. The ovary cannot be enclosed because it must give up its belongings so often. It gives up eggs, yes, but it gives more than that. It gives up a kind of pudding, a yellowish tapioca of hormones that feed the reproductive cycle… The ovary operates as a physiological and allegorical bridge between stasis and sexuality, between anatomy and behavior. Through its hormonal emissions, the ovary makes itself known to us. …

Until girls and boys are three or four, a structure in the hypothalamus called the gonadotropin-releasing hormone pulse generator ticks and tocks and secretes tiny bursts of reproductive hormones. … A girl's ovaries respond to the pulsatile message. They secrete small amounts of ovarian hormones in return. Nothing serious yet, not nearly enough to grow breasts or to ovulate… At the end of toddlerhood, through a mechanism that remains largely mysterious, the pulse generator in the brain shuts down. … The ovaries too fall silent. They retreat into hibernation. For this reason, … the child is likely to turn prudish, to be easily embarrassed by bodily functions… The first glimmerings of renewed care … appear at the age of ten, not as a result of gonadal activity but at the behest of another set of organs: the adrenal glands, blood-rich structures that sit atop the kidneys… The adrenals secrete adrenaline, the fire-under-thy-butt hormone, and they also release small doses of sex hormones. …

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After the adrenals have spoken, there is no turning back… The body will follow the lead of the mind, and it will become sexualized. At the age of twelve or so, the pulse generator in the hypothalamus is resuscitated, disinhibited. It begins squeezing out packets of hormones again. … The revived hypothalamus is stronger now by far than it was in its nursery days. And stronger still are the ovaries, the gray sacks of heirloom pearls. They are ready to roll. The adrenals can go only so far. The ovaries know no bounds. They are the primary source of sex hormones… The sex hormones cause pubic hair to grow, fat to gather on the breasts and hips, the pelvis to widen, and eventually menstrual blood to flow."

Over-the-counter:

Available without a prescription.

Ovulation:

The time when one of the two ovaries releases an egg. When ovulation occurs, the mature egg is released from its protective follicle in the ovary. This process of follicular rupture looks a bit like a small volcano erupting on the ovarian surface. At this time, the tubal fimbria, like tentacles, sweep over the surface of the ovary and actually "swallow" the egg. The egg then has a few hours lifetime (8 to 12 hours or maybe up to 24 hours) in the protective confines of the fallopian tube, for a sperm to swim up and reach it. For the mechanism of ovulation see the web reference at http://www.woomb.org/bom/science/physiology.html .

Ovulation method:

See cervical mucus method. But before you go there, note this: The ovulation method might more accurately be referred to as peri-ovulation method, peri- being the Greek prefix that means around, about, enclosing, or near. From dictionary.com we also learn that in Persian mythology, peri is a beautiful and benevolent supernatural being or fairy, earlier regarded as malevolent. [Persian par, from Pahlavi park, malevolent sprite, from Avestan pairik, a kind of female demon.] But dictionary.com does not have any entry for perimenopause. And bioZhena is introducing a technology with which to remove the peri- from the self-diagnostic detection of the fertile period and ovulation itself.

Ovulona™, The:

This is the putative trade name of the women's health version of the bioZhena device, as opposed to the animal version (see the BioMeter, above). An earlier prototype was once referred to as the Ovulon but the feminine-gender name is surely more appropriate.

Now a citation: A remarkable property of the cervix is the extreme sensitivity to the effect of estrogen and progestogens. Changes in the composition and properties of cervical secretions have been used for many years as an in vivo biologic assay for sex steroids. How well put, on page 564 of the compendium "Human Reproduction: Conception and Contraception", edited by E.S.E. Hafez and T.N. Evans, Harper & Row Publishers, 1973. In the Epilogue, Professor Hafez further states that "…the fertile period of the menstrual cycle is not more than 4 days, and probably less". He also says: "Unfortunately, accurate detection of this fertile period is difficult, due to individual variation in the length of the menstrual cycle and frequency of ovulation, and to the absence of clinical signs of ovulation." We cite him here because the books edited by Hafez were explored at the inception of this project, and because all these referenced facts of life were the premises for the inception of the project and for the development of the intellectual property. You may almost view the cited reference to the remarkable property of

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the cervix as a definition of the bioZhena innovation. "Accurate detection of the fertile period" is the operative phrase, and it is what eludes the various alternative methods and products. Note that those products have not solved the fundamental diagnostic problem of woman- or mankind.

The origination of the Ovulona (and/or BioMeter) technology was a response to this fundamental human need on the part of a husband and wife pair of scientists. On the one hand, we struggled with the newly experienced pain of an apparently sterile marriage. But we also realized that we were conceivably in a position to help ourselves by combining our respective professional resources. It all goes back to the postulate, by the ever so pragmatic female of the species, that before any of the more or less bothersome medical procedures should be undertaken, the basic problem of proper timing (of the intercourse) must be conquered. This is how the project came about, and everything else followed. (The reader will understand that the postulated principle holds for every couple.) And let's be explicit about the fact that "everything else" includes not only the broad applicability of the ensuing tissue biosensor. It also includes the realization that we are monitoring folliculogenesis (the maturation of the egg in the ovarian follicle). And it includes, more importantly, the crucial capability to detect ovulation and not just predicting it.

Although we could not really be clear about this until Chiara Benedetto, M.D. sent us the results of measurements (with an early prototype) of her carefully selected baseline-type subjects, the Ovulona provides not only a short-term anticipation of ovulation but also an earlier long-term prediction signal. This long-term predictive peak really has no counterpart among the various other methods of fertility monitoring. Its position ahead of ovulation apparently depends on the rate of maturation of the dominant follicle in the given menstrual cycle, and it correlates with the length of the menstrual cycle. None of this would have been apparent from the early in-house longitudinal study, since the study involved a non-baseline subject.

Data to date indicate that, with the exception of some rather rare (unusually short) menstrual cycles, the long-term warning of the upcoming ovulation event occurs comfortably early for the practice of natural family planning (NFP). Consequently, we are in a position to claim progress over the 1973 statement in the Hafez Epilogue, which stated that "the long-term prediction of ovulation by at least 6 days seems to be difficult and, as yet, unsolved" (loc. cit. page 711).

The capability to anticipate ovulation well in advance, and to then detect ovulation independently of the predictive signals, is unique to the bioZhena technology. This unique capability results from the mode of action, further discussed under Modus operandi (MO), above. See also under Mysterious conceptions (or the lack of thereof). From the MO also follows the broad applicability of the technology, which is another feature that distinguishes the Ovulona from any other product addressing fertility and ovulation. For a potential impact of the technology on public health, see under Sexually transmitted diseases, and also under Cervical cancer and under Smoking.

It could be argued that the greatest aspect of the bioZhena project is the idea of introducing – via the affordable personal fertility monitoring method – a general, routinely used, women's health tracking and diagnostic tool, with the potential to impact on several important areas of public health. We have every intention to make this argument, and plan to put it into practice.

Ovum (in plural: ova):

The female reproductive cell or gamete of animals; egg.

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Pap smear test:

A procedure used to examine the cells of the cervix in order to detect infection and hormonal conditions. It can also detect precancerous and cancerous cells. The Papanicolaou ("Pap") smear has been the method of choice for cervical cancer screening for over 50 years. The sensitivity limitations of the Pap smear have been well documented, and include an overall false negative rate variously reported as between 20-40%, and between 6-55%. The diagnostic test to evaluate patients with abnormal cervical cytological smear results is colposcopy (see Colposcope, above). We plan that the bioZhena technology will provide an alternative screening, with the advantage that this will be performed routinely by many women at home; abnormal results will be referred, much like the Pap results are at present.

Parturition:

The process of giving birth; childbirth. [From Late Latin parturitio, parturition-, from Latin parturitus, past participle of parturire, to be in labor.] Parturition is illustrated at http://www.mhhe.com/biosci/esp/2001_saladin/folder_structure/re/m2/s5/ . The illustration's legend indicates that physicians usually calculate the gestation period (length of the pregnancy) as 280 days: 40 weeks or 10 lunar months from the last menstrual period (LMP) to the date of confinement, which is the estimated date of delivery of the infant [EDD]. Indubitably, due dates are a little-understood concept: "Truth is, even if you know the exact date when you ovulated, you still can only estimate the baby's unique gestational cycle to about plus or minus two weeks" [http://www.gentlebirth.org/archives/dueDates.html].

Statistically, the gestation time for human babies has a mean of 278 days and a standard deviation of 12 days, an uncomfortably large spread. The old Naegele Rule of a 40-week pregnancy was invented by a Bible-inspired botanist Harmanni Boerhaave in 1744 and later promoted by Franz Naegele in 1812. It is still believed to work fairly well as a rule of thumb for many pregnancies. However, the rule of thumb also suggests: "If your menstrual cycles are about 28 days, quite regular, and this is not your first child, your physician's dating is probably fine. If your cycles are longer or irregular, or if this is your first child, the due date your physician has given you may be off, setting you up for all kinds of problems" (induction, interventions, C-section among them).

This is where the bioZhena technology is expected to provide definitive help, making it possible to reckon the EDD with recorded ovulation data rather than merely with the LMP + 280 days. This may be expected to have a significant impact on obstetric management. It is ironic that, in this age of technological medicine, American women worry about their birthing process not being allowed to take its own natural course on account of an ancient method of predicting the EDD. Ironically, the 40 week dogma - which is the gestational counterpart of the calendar method of birth control – does not reconcile the 295+ days of the 10 lunar months; and yet, at the same time, the U.S. has an unusually high perinatal death rate, resulting from high statistics of too early (preterm) labor. Quid agitur? See also under Gestation.

Parturition alarm:

This is a concept that has to do with the need to know when labor or delivery is beginning, because the birthing female may be in need of help. At this writing, an Internet search has produced only one such technology, a pressure-sensing girth, suitable for the horse breeder only, because it utilizes the fact that the horse mare lies on her side only in the process of

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parturition. In that paper, reference was made to some other method that would detect the emergence of the amniotic sac or of the foal from the vulva (vaginal orifice) but that was not a satisfactory solution. In the horse-breeding arena, about 5-6% of births require help. In human obstetrics, where most births take place in hospitals, determining the right time of confinement would be beneficial. bioZhena will investigate the vaginal sensor technology with a view to developing a parturition alarm applicable to any mammal.

Pearl Index:

A measure of contraceptive efficacy for comparisons of different methods of birth control. Defined as the number of failures per 100 woman-years of exposure. In Germany, microprocessor-thermometer aided NFP was found to have Pearl Index of 0.7, comparable with that of the Pill and far superior to other artificial contraceptive methods, as follows: Pearl Index of the Pill = 0.5 - 1; Pearl Index of the spiral IUD = 2 - 4; Pearl Index of barrier methods (condoms, diaphragm, ...) = 5 - 15.

Pelvic exam:

Physical examination of the vulva, vagina, cervix, uterus, and ovaries — usually includes taking cervical cells for a Pap test and a manual exam of the internal pelvic organs.

Pelvis is the structure supporting the lower limbs in humans and the hind limbs or corresponding parts in other vertebrates [synonyma: pelvic girdle, pelvic arch, hip]. It is a basin-shaped structure of the vertebrate skeleton, composed of the unnamed bones on the sides, the pubis in front, and the sacrum and coccyx behind. The structure rests on the lower limbs and supports the spinal column. Pelvis is the cavity formed by this structure. [From Latin pelvis, basin.]

Manual exam or palpation is a method of examination in which the examiner feels the size or shape or firmness or location of something (of body parts when the examiner is a health professional). [From Latin palpare, palpatio, to touch gently.]

Perfect use:

The contraceptive effectiveness of a method for women and men whose use is consistent and always correct.

Perimenopause:

The period of change leading to menopause. The kind of healthcare controversies and decisions faced by women at this stage of life is illustrated by the discussions at http://www.oxford.net/~tishy/longtermhrt.html (go to HRT – Long term considerations).

Perinatal:

Relating to the period around childbirth, especially the five months before and one month after birth: as in perinatal care. Also prenatal or antenatal. These two terms are actually more specific because they do not include the one month after birth, but the term perinatal appears more frequently used. Note: peri- is a prefix meaning 1. around, about, enclosing; or 2. near: as in perinatal [Greek peri: around, near + from Latin natalis, pertaining to birth.]

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Periodic abstinence:

Not having intercourse during the "unsafe days" of a woman's fertile phase in order to prevent pregnancy. This differentiates NFP from FAM. For more about periodic abstinence, see under Rhythm method.

Phases of the menstrual cycle:

The pre-ovulatory phase is called the follicular phase (during which the dominant follicle is maturing towards ovulation), and the postovulatory phase is called the luteal phase (dominated by the corpus luteum into which the now-empty follicle has transformed).

PID (pelvic inflammatory disease):

An infection of a woman's internal reproductive system that can lead to sterility, ectopic pregnancy, and chronic pain. It is often caused by sexually transmitted infections such as gonorrhea and chlamydia.

Pill, the:

Common expression for oral hormonal contraception. Also called oral contraceptive (OC). This is how the Pill works: The Pill contains steroid sex hormones. There are basically two general types of the Pill: 1. progestogen (synthetic progesterone analog) only, called the mini-Pill, and 2. combined progestogen-estrogen (combined Pill). One effect is to suppress the triggering mechanism in the brain, which causes the release of the gonadotropin hormones FSH and LH, and thus to prevent ovulation. The combined Pill suppresses ovulation in about 98% of cycles. The mini-Pill suppresses ovulation in about 40% of cycles. The Pill also affects the natural functioning of the endometrium and of the cervix. The effect on the endometrium is to disrupt the normal growth pattern so that it cannot sustain an embryo. Progestogen stimulates the production of the kind of mucus that prevents sperm penetration and sperm survival. Web reference: http://www.billings-ovulation-method.org.au/act/pill.html .

Recognition of anti-fertility effects of ovarian secretions was recorded more than a hundred years ago (1898) by Beard in Edinburgh, followed by numerous papers in European literature that set the stage for the development of the Pill. In America, Selye et al. (1936) and Makepeace et al. (1937) proved the ovulation-inhibiting effects of progesterone in rodents, and Sturgis and Albright (1940) demonstrated the clinical inhibition of ovulation through the cyclic use of estrogens. The first 19-nor steroids were synthesized by Ehrenstein at the University of Pennsylvania in 1944, and later found to be more potent progestational agents than progesterone. The logical extension of those studies did not occur until early 1950s, largely because of shifts in R & D during World War II: Pincus at the Worcester Foundation for Experimental Biology in Shrewsbury, Massachusetts, and Rock with Garcia at the Free Hospital for Women in Brookline, Massachusetts. Colton synthesized norethynodrel at the Searle Laboratories, and Djerassi synthesized norethindrone at Syntex in the early 1950s. The FDA approved the Pill in 1957 for non-contraceptive uses and in 1960 for contraception. The sequential regimen was introduced in 1963. Since then "the Pill" has meant a rather wide array of progestogens and estrogens prescribed in combined or sequential formulations.

According to Carl Djerassi, one of the creators of the Pill, the capitalized name of the Pill was coined by Aldous Huxley in a 1958 collection of essays entitled "Brave New World Revisited". Here is the Huxley quotation: "Most of us choose birth control – and immediately find ourselves confronted by a problem that is simultaneously a puzzle in physiology, pharmacology,

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sociology, psychology and even theology. The Pill has not yet been invented." More interesting is that Djerassi, the author of, among other things, "The Politics of Contraception", says the following in "The Pill at Forty: What Now?" chapter of his 1992 autobiography. [QUOTE from The Pill, Pygmy Chimps, and Degas' Horse, page 259:] If I were restricted to choosing a single new contraceptive, it would be a once-a-month pill effective as menses inducer [a chemical inducing menstruation]. Instead of the current oral contraceptive, which a woman takes daily… a woman would take, at most, 12 pills annually, rather than the present 250 or more, and would not know in any month whether her egg had been fertilized [END OF QUOTE].

If this sounds like a recognition of the seriousness of the chemical interference with the natural functioning of the body, it is a fact that this "Father of the Pill" has become an advocate of fertility awareness or natural family planning. Surely, it is interesting that the creator of the Pill declares that he "would focus on a potentially much wider customer base under the banner of fertility awareness." And he is "thinking of the many women who now feel strongly about health awareness and about making more health-related decisions by themselves… For many a woman in our affluent society, knowing whether and when she is ovulating should be a routine item of personal health information, which could have advantages quite separate from birth control." Touche!

Djerassi goes even further: "And finally, why not employ such methods of ovulation detection and prediction as routine teaching tools in high schools? Emphasis on fertility awareness rather than on birth control might be an effective strategy to fight the continuing politicization of sex education in American high schools. Who knows? It might even lead to a reduction in unwanted pregnancies." An unexpected proposition coming from someone who was once intimately involved with the creation of the Pill? The Stanford professor of chemistry and former key employee of Syntex Research has become a science-in-fiction writer while occasionally teaching courses on biosocial aspects of and feminist perspectives on birth control. He draws attention to the quotation by Margaret Mead: "The Pill is entirely the invention of men. And why did they do it? … Because they are extraordinarily unwilling to experiment with their own bodies … and they are extremely willing to experiment with women's bodies … It would be much safer to monkey with men than to monkey with women … Now the ideal contraceptive undoubtedly would be a pill that a man and a woman would have to take simultaneously." Well, this too is a part of the story of the Pill at forty plus.

The rest of the story is in the 1995 book by Bernard Asbell, "The Pill - A biography of the drug that changed the world". Asbell tells about the complicated history of the development, including the less than friendly relationship between the two creators of the Pill's chemicals, the other one being the chief research chemist of G.D. Searle, Frank B. Colton. While Djerassi and Syntex applied for a patent in November 1951, Searle did not file until August 1953, and "for forty years Carl Djerassi was not to let go of a misgiving that, in claiming a patent of its own, Searle was poaching. The similarities between their two drugs raised exquisite legal issues. Searle's norethynodrel was so similar to Syntex's norethindrone that, according to Djerassi, mild treatment of Frank Colton's norethynodrel with hydrochloric acid or, in fact, even so weak an acid as human gastric juice, converts it to a large extent into [Djerassi's compound] norethindrone. Which, Djerassi says, raises this enchanting question: When the natural processes of the stomach 'synthetize' a patented compound, is that an infringement of an issued patent?"

Asbell describes the circumstances surrounding the FDA approval in 1957 of both the Syntex-Parke-Davis's drug Norlutin, as well as Searle's Enovid, with "the approval limited, of course, to treatment of disorders." He describes the big pharmaceutical companies' involvement or non-involvement with the pioneering Syntex (started originally by a Pennsylvania maverick, basic research steroid chemist Russel Marker), and how later a Syntex executive said "ruefully, 'Through the mid-fifties we were busy fools selling vast quantities of raw materials for other

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people to make a profit out of.' The various controversies and conflagrations are described, and how these "did not appear to trouble the new Wall Street owners of Syntex, while at Searle … decision makers found themselves gripped by the traditional competing pulls of temptation and fear." A Syntex board member at the time is quoted saying, "…when you have something that changes the approach functionally and esthetically, then all bets are off. We didn't underestimate its potential. We didn't know *what* to estimate." Carl Djerassi joined Syntex in 1949 at age 26, "yearning to try his hand at the hottest field of research in steroids… In 1956, a New York investor … ignored the contrary advice of his lawyer … and bought Syntex, [acquiring] Syntex's patents and the talents of Carl Djerassi and George Rosenkranz". The latter had invited Djerassi to join them, and later Rosenkranz became the CEO of the new Syntex Corporation. Djerassi left Syntex for Stanford University in 1960. According to Colton, in 1950 Djerassi's Ph.D. supervisor at the University of Wisconsin told Djerassi, as well as another one of his former students who was now at Searle, about a synthetic process he was working on, and which was subsequently developed into new progestins (or progestogens) at both Syntex and Searle, somewhat as though in parallel.

Asbell tells how, eventually, Searle decided to go out on what someone called "the longest limb in pharmaceutical history", when they decided to file an application to license Enovid as a contraceptive, based on field trials with less than a thousand women "who had been 'on the Pill' for 10,427 cycles". He describes how Syntex signed a contract giving the Ortho division of Johnson & Johnson the marketing rights to norethindrone; but, because their earlier license holder Parke-Davis refused to release some research results, Ortho did not receive the FDA approval to market Syntex's norethindrone until 1962 (under the trade name Ortho-Novum). This was two years after Searle's product launch in May 1960. Asbell's narration is instructive, such as when he cites an FDA person saying, "The important things to us at the FDA were quality control, purity of product and side effects." While Syntex was losing two years, Searle played its advantage: Searle's sales totaled $37 million in 1960, just before the FDA approval of the Pill, and "they soared to $89 million in 1965. But once Syntex fully entered the race, its stockholders profited at a rate virtually unprecedented in the history of the stock market… When its sales multiplied from $7 million to $60 million, its earnings per share of stock ballooned from three cents to two dollars. To avoid certain costly tax hazards, most of the shares had been sold or given to key employees of Syntex, research director Carl Djerassi, as noted, among them. The shares, originally valued at two dollars each when issued, were soon traded at eight to ten dollars each. Before long, the price reached three hundred dollars a share, then split three for one … An original single share thus fissioned by 1993 into 192 shares, exploding the value of an original two-dollar share to eight thousand dollars."

Asbell also comments: "By this time, Russel Marker, whose original discovery of the treasure in a lowly yam had made all those riches possible, was long gone from the scene of his handiwork, gone from chemistry and, for all any of his former colleagues knew, dead broke." A generation later, Marker was asked whether serendipity had played a major role in the discovery. "The genius alchemist of synthetic progesterone (who was apparently betrayed by Dr. Somlo, his principal partner at the infant Syntex Corporation) … declared: 'Serendipity? Hell, no!' Nor had Marker, the classic "basic" researcher, been driven by a vision of an end product. He has asserted [to writer Bernard Asbell]: 'I was never interested in the *use* of the hormone, only in making it available… I didn't realize it could be used for birth control pills until I had quit completely.'" But then, Asbell writes, having described the general steroid chemistry bandwagon of the time, "… recalling the exquisite conquest years later, Djerassi was to say, still again, 'Not in our wildest dreams did we imagine that eventually this substance would become the active ingredient of an oral contraceptive'. Djerassi had not the faintest knowledge that, less than a year earlier, Margaret Sanger had dined with Gregory Pincus in New York to reveal her vision of a 'perfect contraceptive', nor that both Sanger and Katharine McCormick [a wealthy widow with a strong conviction] would soon visit Pincus at Worcester to seal their pact

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to search for one." Then again, Colton too asserted that he had initially no idea that his Searle group was creating a contraceptive compound.

Pincus was a talented reproductive physiologist (he had pioneered in vitro fertilization in experimental animals) who, having been recruited by the two driven women, became – along with the gynecologist John Rock – one of several candidates for the title of "The Father of the Pill". His story is told in a chapter with the enchanting title, "In science, Lizuska, everything is possible". Gregory Pincus was the "technical entrepreneur who pursued the innovation in the face of opposition or indifference by fellow scientists, or despite predictions by businessmen that the product would fall flat in the marketplace… He drew G.D. Searle and Company into the project while other drug houses were refusing to consider marketing a contraceptive." Later on, "Searle officials even considered a plan to copyright the words 'The Pill' as a trade name" – but it was an idea they apparently only toyed with. "Although the Pill enormously fed and fattened the G.D. Searle Company, its arrangement with Pincus called for not a penny of royalty to him or the Worcester Foundation." On the initiative of the Chang widow, the tombstone of Gregory Pincus' chief research operative now carries an engraving: M.C. Chang, The Father of the Birth Control Pill.

A LITLE POSTSCRIPT

If you were to pick up Carl Djerassi's 1998 book "NO", you would find a story of a protagonist modeled in part on yours truly, and our former company in Colorado, now defunct. (Nice country, Colorado, and some nice people, like everywhere else. Others, a bit too much of the cowboy culture, harking back to the range wars, perhaps, of two centuries ago.) NO is thus named for nitric oxide. "Although one of the simplest biological molecules in nature, nitric oxide has found its way into nearly every phase of biology and medicine, ranging from its role as a critical endogenous regulator of blood flow and thrombosis to a principal neurotransmitter mediating erectile function, to a major pathophysiological mediator of inflammation and host defense."

However, the reason for this post scriptum here is to share with you that, on his web site (http://www.djerassi.com/noeng.html), Djerassi says the following about his book: "Since my own scientific contributions in reproductive biology have focused on women rather than men, I could not resist introducing a second biotech development involving ovulation prediction - a current focus of my teaching at Stanford University. The electrochemical approach, and the fictitiously named Wizard of Ov described in this novel, are based in part on very recent developments of Conception Technology Inc., in Fort Collins, Colorado. But the same caveat applies here as well: I take no responsibility for any child's paternity or any failure in sex-predetermination based on the use of this novel's Wizard." [END OF QUOTE]. Needless to say that we at bioZhena know better than "to be asking" for any litigation, paternity or otherwise.

Porcine:

Of pigs or swine. Porcine data from:
http://mark.asci.ncsu.edu/Swine_News/2000/sn_v2307.htm :
[For efficient pork production], there are four factors: sperm and oocyte longevity in the female reproductive tract, estrus detection frequency, and projected estrus length for determining when and how often to breed to accomplish this is determined.
The fertile life span of a spermatozoa population in the female with the ability to produce a pregnancy is estimated to be from 12 to 36 hours, even though motile sperm have been recovered 10 days following insemination. The fertile life span of the ovulated egg is approximately eight hours.

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Good fertilization rates (> 90 percent) can be achieved when a single insemination is performed during a 24-hour period before ovulation. This optimal "AI time" is assuming that 1) an adequate number of sperm are inseminated and retained, and 2) semen is relatively fresh (less than 38 h old). This interesting finding would suggest that all producers need to do is determine when ovulation is going to occur and inseminate the sow. It is unfortunate however that, on average, ovulation takes place 35 to 45 hours after onset of oestrus (standing response in presence of a boar) but the variability between sows is extremely large, thus making it difficult to accurately time a single insemination. Therefore, performing multiple inseminations throughout estrus is an easy answer to increase the chances that one insemination will be performed at an "optimal time." Although it is difficult to predict ovulation, research has shown that sows generally ovulate sometime during the last half of their estrus period. [END OF QUOTE]

According to Don Hoglund, DVM, porcine fertility is a particularly attractive target for the bioZhena technology, since one can not palpate a sow as one can a mare or a cow. Palpation, of course, allows the technician to feel the ovary and get a "fairly accurate" sense of approaching ovulation. Sperm life span is the window of opportunity for hand palpation. In swine, though, there is no such method as palpation. Yet, swine production is at an all time high, worldwide. Animal pharmaceutical companies are looking to sort semen and to predict 'one-time' breeding schedules (pigs breed 2-3 times per year) and/or to predict ovulation more reliably. Dr. Hoglund, who is also an MBA economist, argues that these companies will sink large sums into this project. Why? They want to capture the pig producers' 'other' drug needs: feed additives, antibiotics, vaccinations, etc. The profit potential for the pig-farmer is in labor reduction when capturing labor-cost savings from not having to re-breed a sow. That may be the only profit in the production cycle.

Pregnanediol:

A metabolite (breakdown product) of progesterone, excreted in the urine.

Premenstrual syndrome (PMS) and PMDD:

PMS is a combination of emotional, physical, psychological, and mood disturbances that occur after ovulation and normally end with the onset of the menstrual flow. The symptoms include abdominal bloating, breast tenderness, headache, fatigue, irritability, anxiety, and depression. At least 30% of menstruating women experience distressing premenstrual symptoms that compel them to seek their doctor's help, and as many as 60% to 75% of women experience some of the PMS symptoms. Of these, about 2% to 10% experience severe problems and functional impairment, which is called the premenstrual dystrophic disorder or PMDD.

According to the PMS expert, Joseph Mortola, PMS is one of the most common disorders treated by reproductive endocrinologists. Diagnosis depends on prospective recording of symptoms and a documented symptom-free interval during the follicular (premenstrual) phase of the menstrual cycle. PMS/PMDD is an entity that can be distinguished from (and treated differently than) anxiety disorders and depression. However, the research is still in its infancy. According to Dr. Mortola, the realization of the effectiveness of certain new drugs such as the GnRH analogs combined with estrogen/progestin replacement therapy is an important area for future research, where the optimal dosages of replacement therapy have yet to be determined. This is similar to the situation with perimenopausal HRT.

Therapeutic treatment of PMDD, in particular, requires to ascertain whether the symptoms are unique to the premenstrual phase or not. This is to differentiate PMDD from clinical depression, for proper treatment. Current medical practice (both primary care and particularly psychiatry,

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which steps in once the primary care fails) utilizes nothing better than the discredited calendar-based rhythm method rather than a rigorous technique for ovulation detection. The bioZhena technology should have a positive effect in that arena. Two key words are pertinent in this context, namely psychoneuroendocrinology (or even psycho-neuro-immuno-endocrinology) and the much shorter psychosomatic, as in psychosomatic medicine.

Progesterone:

A hormone produced in the ovaries of women that is important in puberty, menstruation, and pregnancy. It is produced by the corpus luteum in the ovary upon ovulation. It is also responsible for the post-ovulation rise in the BBT, and for the change in the cervical fluid and cervical position in the postovulatory infertile phase. Progesterone is also an important precursor in the biosynthesis of adrenal corticosteroids (hormones that protect against stress) and of other sex hormones (testosterone and estrogen). Besides being a precursor of other hormones, it also facilitates many other important physiological functions. In addition to the ovaries, it is also secreted by adrenal cortex, and by the placenta. Progesterone is an essential hormone that plays a part in the development of healthy nerve cells, and brain and thyroid function. Also, progesterone stimulates osteoblast-mediated new bone formation.

Progestogen or progestin:

Any synthetic progesterone analog (structural derivative). Used in contraceptives to inhibit ovulation, and in hormone replacement therapy (HRT) for menopausal women. Progestogens counteract the cancer-promoting effect of estrogen in HRT, but the actions of progestogens differ significantly from natural progesterone in other respects. Focusing on the contraceptive use, there are numerous birth control Pills on the market, and a given brand of the Pill can be either estrogen dominant, progestogen dominant, or androgenic (testosterone-like male hormone effects), depending on the actual doses of the components and their relative potencies. This is only a relative classification that does not hold from one woman to another. Each progestogen has a different potency in terms of the progesterone effect to stop menstrual bleeding, or the androgen effect to stimulate acne and hair growth, or a partial estrogenic effect.

It is interesting to note that the progesterone analogs and estrogen are electrochemically related (estrogen is reduced progesterone, where electrochemically reduced means electronated and hydrogenated). Indeed, bioconversion of the 19-nor progestins to their corresponding tetrahydro derivatives results in the loss of progestational activity and acquisition of estrogenic activities. Many experts believe that the side effect differences between different contraceptive formulations are not consistent because all contraceptives have been greatly reduced in dose from when older data on higher dose Pills were examined. Others agree that the various side effects (e.g., weight gain, feeling tired, fluid retention, breakthrough bleeding, nausea, depression, and numerous others) have been reduced but they are still manifest in some women, depending on the doses of the components in a given Pill formulation. Further information can be found at: http://www.wdxcyber.com/ncontr13.htm . Then, a pharmacy site, http://www.rxlist.com/cgi/generic/medrox_ad.htm , states (among other things): A statistically significant association has been demonstrated between use of estrogen-progestin combination drugs and the following serious adverse reactions: thrombophlebitis; pulmonary embolism and cerebral thrombosis, and embolism. For this reason patients on progestin therapy should be carefully observed.

The Medscape.womenshealth.com newsletter carries the following advertisement: "Mistakes happen, that's why there's Plan B. Plan B is the first progestin-only emergency contraceptive to be approved by the United States FDA. Plan B is safe and highly effective. The first tablet

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must be taken within 72 hours of unprotected intercourse. Let your patients know that if Plan A fails, there is a Plan B."

R

"Rhythm" method:

Also called the calendar method, it has been discredited because of two factors: its unwarranted assumption of regularity of menstrual cycles, and the long period of abstinence demanded by it. The method's one-time well-known status has caused a skeptical bias in America to all NFP or FAM methods, although they are very different.

S

SALIVA TESTING FOR FERTILITY STATUS:

This is a somewhat "low tech" approach to fertility testing, which would normally hardly deserve an entry here, because of its attributes. However, the media recently carried an announcement of the FDA having approved a salivary testing device, and a number of people interested in our project have asked us about it. From our perspective, this is one of those news events that show public interest in self-diagnosis of fertility. This never-ending consumer interest is a basic premise of the bioZhena business plan. Saliva testing would not be found in any large-scale scientific studies of natural family planning or of fertility issues. In fact, salivary testing typifies the shortcomings of surrogate indicators of fertility status, since it involves a physiological property remote from the mechanism of ovulation, an indirect and inaccurate estimate of the fertility status. It nevertheless offers an inexpensive alternative.

Suffice it to cite from the web site of Craig Medical Distribution Inc. ("Quality Medical and Forensic Diagnostics Since 1984") at http://www.craigmedical.com/ovulens.htm : "…just prior to ovulation, electrolytes (or salts) increase dramatically in body fluids (e.g., cervical mucus and saliva) along with the hormone estrogen. Consequently, being able to identify this increase in electrolytes (salts) is an alternative method for identifying the onset of ovulation. Historically, it has been clinically and scientifically observed that, during the fertile period, a sample of normal female saliva or cervical mucus - when dried and examined under a microscope - contains many structures resembling ferns. These fern structures are actually dried salt or electrolyte crystals present as a result of the electrolyte build up prior to and during ovulation. On all other days of the female cycle, only shapeless dotted structures can be seen. This natural phenomenon has been known for many years to researchers and medical professionals. However, a precision miniature microscope designed specifically to aid in the indication of the fertility period is now available. Any woman can now easily check her fertility cycle anytime, anywhere without the need for basal charting or urine samples. Saliva is the most accessible body fluid and easiest to obtain. There is no need for complicated blood or urine tests. 'Fern' structuring starts 3-4 days before ovulation and ceases 2-3 after ovulation."

Thus, saliva monitoring amounts to a peri-ovulation method tool, as discussed above (see under Ovulation method), and which relies on subjective judgment of the user.
There are a number of inexpensive fertility-testing microscopes on the market today, as well as at least one rather costly device that measures the conductivity of saliva (from Zetek, Inc., referenced in the bioZhena business plan). The reader will understand, having reviewed this glossary-primer, that hormone monitoring (indirect at that) is not the same as monitoring the

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actual fertility status. Having a qualitative indication of the elevated levels of estrogen in body fluids is a far cry from the quantitative determination of the beginning and the end of the fertile period.

Sexually Transmitted Disease (STD):

Any of various diseases, including chancroid, chlamydia, gonorrhea, and syphilis, that are usually contracted through sexual intercourse. Some 56 million Americans have an STD other than AIDS and many more are infected each year. The causative bacterial, viral, or parasitic agents are spread primarily by sexual contact, but may also be spread by the use of infected needles. Some STDs are chronic infections, but many can be cured. Early diagnosis and treatment are often the keys to the cure. However, one problem is that many cases of these infections are asymptomatic and thus go undiagnosed. The only 100% effective prevention of STDs is sexual abstinence. Maintaining faithful monogamous relations with one's spouse is effective, provided both partners are free of STDs. Safe sex (use of a condom) with a monogamous partner is the next best protection against STDs.

Much like the chemical contraception, the bioZhena technology cannot protect against the microbial agents causing STDs. However, there is a fundamental difference between the chemical contraceptives and the Ovulona™ of bioZhena, which the reader should contemplate and appreciate. The following paragraph should be read slowly and carefully.

The Pill was instrumental in the so-called sexual revolution of a few decades ago, and was particularly effective in substituting sexual promiscuity where social mores used to be controlled by puritan outlook on life. It is the sexual promiscuity that has resulted in the upsurge of STDs. The Ovulona will not be part of the same scene, on the contrary. Since our device is a tool for Natural Family Planning (NFP), and since the requirement of certain sexual discipline is inherent in NFP as well as in the use of the Ovulona, bioZhena Corporation is poised to make a positive contribution to public health. This will include particularly the important reduction in the prevalence of STDs - by encouraging and assisting the NFP method of birth control. As always, prevention is the sensible approach to disease control, and a contribution to the reduction in the extent of promiscuous sexual encounters is a definite contribution to public health. That, quite apart from the basic reproductive-management application of the bioZhena technology, holds the key to the significance and potential of what we have to offer. In addition, we will also investigate the likely possibility that the effect of these infections on the vaginal tissues is such that a distinct signature may be generated in terms of the menstrual cyclic profile, providing an early warning of a pathological state. Thus, our participation in a two-pronged attack on this scourge of present-day America can be envisaged.

You will have learned (under Fallopian tube, above) that, in fact, the renaissance-era inventor of the condom, Gabriel Fallopius, developed the device not for birth control but for the prevention of sexually transmitted diseases. Here is more about the seriousness of the STD threat to public health. Some 5.5 million new cases of the Human Papilloma Virus or HPV infection are reported each year in the U.S. Twenty million Americans, men and women alike, are infected with this virus. In women, the infection may be vaginal or cervical. If the cervix becomes affected, cervical cancer can result. The Herpes Simplex Virus (HSV) causes a recurrent, incurable viral disease that has two forms, HSV-1 and HSV-2. HSV-1 generally appears as cold sores around the face, especially the mouth. HSV-2 is a sexually transmitted disease that manifests as genital lesions. As many as 50% of patients with genital herpes shed the virus without experiencing any symptoms. There is no cure for herpes, only a few drugs that will help shorten the duration of the symptoms and relieve the discomfort associated with herpes.

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Then there is the Human Immunodeficiency Virus (HIV) and Acquired Immunodeficiency Syndrome (AIDS). HIV is the virus that causes AIDS. Some 900,000 Americans are currently estimated to be infected with HIV, with about 40,000 being added each year. Compare this 0.9 million number with the 56 million Americans that have an STD other than AIDS.

Among the bacterial STDs, gonorrhea ("clap") is a common disease worldwide, and females are twice as likely to become infected after one act of intercourse with an infected male as males are after one act of intercourse with an infected female. Chlamydia is the most frequently reported and fastest spreading STD in the United States. More than 3 million men and women in the U.S. are diagnosed each year. Pelvic inflammatory disease is a complication of gonorrhea or chlamydia. It is an infection that generally involves the uterus, fallopian tubes, the pelvic area. Then, there are more than 70,000 new cases of syphilis each year in the U.S. The risk of infection with syphilis after a single exposure is approximately 50%.

STDs are clearly diseases worth trying to eradicate from human experience. Treatments for syphilis were developed over the centuries, some more effective than others, with the hope of finding the 'magic bullet' that would end the suffering. Treatment of syphilis has altered the way STDs affect humanity. By 1560, the time of Fallopius, leper colonies were being set up throughout Europe specifically for people with venereal disease. In the 1690s, as the epidemic slowed down a bit, hospitals were the place for most syphilitic patients. The treatment of choice at this time was mercury, the earliest treatment for syphilis. Ore cinnabar, a form of mercury, had been used in the 1300s for the treatment of various skin diseases, including leprosy. Giorgio Sommariva of Verona was the first person on record to use mercury to treat syphilis in 1496. Jacopo Berengario da Carpi became famous in Italy soon after this first treatment for successfully administering mercury to syphilitic patients. Mercury was used in the form of ointments, oral administration, and vapor baths. Such treatments remained popular for three centuries. In the 1800s, mercury was used so liberally to treat nearly any ulcer found, that many patients were more injured from the treatment than from their ailment.

The next chemical treatment to be developed specifically for syphilis was potassium iodide, in the 1840s. The treatment was amazingly effective, even on patients with later stages of the illness. Mercury had been only moderately effective on late stages of syphilis and was not effective on very deep lesions. The introduction of potassium iodide gave people new hope that there could be a better cure in the future. It set the stage for the introduction of Paul Ehrlich's "silver bullet" cure Salvarson, and later penicillin. Over time, the focus in dealing with syphilis has gone from finding better treatment to finding better preventative measures. For more details, see http://www.i-std.com/ . For more information on AIDS, go to http://www.critpath.org/aric/ .

Sex ratio:

The proportion of males to females in a given population, usually expressed as the number of males per 100 females. For a graphic review of the historically changing sex ratio in the U.S. (1790 – 1990), go to http://www.ac.wwu.edu/~stephan/Animation/sexratios.html .
View this in the context of the following. The website http://www.ourstolenfuture.org/NewScience/reproduction/sexratio/sexratio.htm discusses the changes in human sex ratio:

Usually, the sex ratio (numbers of boys born divided by the numbers of girls born) is slightly greater than one. In fact, world wide about 106 boys are born for every 100 girls. This number is also reported as the male proportion of total births, or 106/206 = 0.514 = 51.4%. Several researchers, however, have reported apparent recent declines in the proportion of male births, in the US, Canada, Denmark and the Netherlands. These declines have been very small but statistically significant. Fewer boys are being born than would be expected on the basis of the

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recent historical worldwide average. For further information: http://www.google.com/search?q=sex+ratio&hl=en&start=10&sa=N . See also under Fetal sex pre-selection, above.

SMOKING (OR TOBACCO AND WOMEN):

Cigarette smoking is the number one preventable cause of death in women in the United States. Of the more than 140,000 women who die prematurely from tobacco-related illnesses each year, 80 percent began smoking while they were adolescents. Evidence demonstrates that those young people, who begin to use tobacco, do not understand the nature of the addiction. As a result, they believe they will be able to avoid the harmful consequences of tobacco use. When most girls begin smoking, they are usually caught up in the immediate experience of what appears to be a "cool", "adult", or even "glamorous" behavior. They are naive about the powerful addictive nature of nicotine, which, for some adolescents, takes hold after only a few cigarettes. Of those adolescents who have smoked as few as 100 cigarettes in their lifetime, most report that they would like to quit, but cannot. Data show that 76 percent of young women-smokers (ages 12 to 24 years) say they feel dependent on cigarettes. Among those who had tried to quit smoking, 82 percent were unable to do so. Tobacco use by adolescent women is a public problem of enormous magnitude that exacts a tremendous cost on the health of our Nation's youth today and tomorrow. This has been quoted here from the web site of Dr. Susan J. Blumenthal, M.D., M.P.A., Deputy Assistant Secretary for Women's Health (http://www.inwat.org/young.htm).

It is estimated that about 30% of deaths from cervical cancer is caused by smoking. Smoking and taking the Pill in combination can increase the risk of heart disease by up to ten times. Smoking while pregnant has serious effects on the health of the baby. Untold adverse consequences affect the lives of those children and the people around them. Tobacco smoke does not discriminate, and this holds whether smoking is active or passive. Lung cancer, heart disease, and chronic bronchitis end the lives of up to 50% of smokers, irrespective of whether they inhabit a female or male body. However, there are a number of serious health effects specific to women. This is why the subject is broached here. (Sources of citations and statistics can be found at: http://www.ash.org.uk/html/conduct/html/tobexpld8.html).

We have preliminary evidence on how the smoker's lifestyle affects the bioZhena (Ovulona) menstrual cyclic profile. These are certain quantitative changes in the cyclic profile, which qualitatively remains much like that of a healthy non-smoking woman (displays the same features). We can envisage that a woman trying to quit smoking may be helped in her endeavor by the bioZhena device. The Ovulona could be prospectively proffered for that purpose as a kind of biofeedback tool. It is envisaged that tobacco interference with the fertility cycle may be recognized and accepted as a powerful motivator in the hard battle with the extremely strong addiction. The magnitude and public health potential of such a goal is not to be underestimated, just like the difficulties lying in that path.

Here is the vision of the future formulated in 1982 by a tobacco industry trade journal called the Tobacco Reporter: "… Women smokers are likely to increase as a percentage of the total. Women are adopting more dominant roles in society: they have increased spending power, they live longer than men … they seem to be less influenced by the anti-smoking campaigns than their male counterparts. All in all, that makes women a prime target as far as any alert European marketing man is concerned. So, despite previous hesitancy, might we now expect to see a more defined attack on the important market segment represented by female smokers?" And, randomly selected, an excerpt from a letter received by the tobacco company RJR in January 1991: "Dear Sirs, You are sending Christmas cards and coupons to encourage my 15 year old daughter to smoke. Please remove my daughter from your mailing list."

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A 1989 document from the tobacco company BAT, titled "Assessment of the Female Target Audience", divides women into blue blouses and white blouses: "The attached article describes the necessity of segmenting the female market. Of most interest is the segmenting of 'blue blouse' versus 'white blouse' working women.
Blue Blouse (traditional working women):
Less educated (high school or less/ some college).
Lower salaries (less than $15,000).
Most likely to have secretarial/clerical job type.
Work to supplement family income.
Desire to be pampered, i.e. inexpensive cosmetics/costume jewelry).
In quantity, the "blue blouse' segment represents the majority of all working women.
White Blouse (career women):
Higher salaries ($30,000 and up).
Work for personal challenges/rewards/self-expression and growth through careers.
Desire for identity and sense of self.
Acquire additional education.
Committed to their careers.
Concerned with professional appearance - upscale attire."

The tobacco industry spends vast sums of money each year on persuading people to take up or continue smoking. In its own words, the industry is "a monster which has to be fed". The industry sees women as a territory to be conquered, and a large portion of the total marketing expenditure is aimed in their direction. Statistics on cessation, uptake and disease reflect this effort. Smoking rates among young women in countries such as the US, the UK and Australia show that, more than any other group, female teenagers are not responding to public health messages. The smoking rates, measured in these population groups, are either increasing or are decreasing more slowly than in any other population group.

The younger an adolescent is when she begins to smoke, the more severe her nicotine addiction is likely to be. Additional health effects of smoking are: respiratory problems (and decreased physical fitness), dental problems (including periodontal degeneration), coronary artery disease, mental health effects (including nervousness, depression, more high-risk behavior, etc.), health-damaging behaviors, and other negative effects on quality of life (bad breath, wrinkled skin, stained teeth, and other negative effects that influence how she looks and feels). Smoking by women in the United States is associated with almost as many deaths from heart disease as from lung cancer, more than 61,000 each year. In 1995, lung cancer killed 62,000 women; of those deaths, 47,182 (76 percent) are attributable to smoking. (Compare this to the 4,400 deaths per year caused by cervical cancer.) In addition to lung cancer, tobacco use is a major risk factor for cancers of the mouth, throat, esophagus, kidney, pancreas, bladder, and cervix.

Perhaps you might take notice of these notions whether you are or are not a smoking adult. Whereas the tobacco lawyer might well dismiss the Ovulona by recognizing it for what it is, a generalized women's health monitor, and what could smoking have to do with fertility and menstrual cycles, anyway?

Smoking is damaging to women's reproductive health. It is associated with infertility, complications during pregnancy, and an earlier onset of menopause. The estimated 20 percent of pregnant women who smoke during their pregnancies subject themselves and their fetuses and newborns to significant health risks, including miscarriage, stillbirth, pre-term delivery, low birth weight infants, and higher rates of infant mortality.

Here is, as an example, the abstract of one of the publications found upon searching the National Library of Medicine for fertility AND smoking. "Smoking and ovarian fertility", by R.

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Wainer, in Gynecol. Obstet. Fertil. 2001 Dec; 29(12): 881-7 [Article in French]: "Smoking reduces the natural fertility, and the delay to conceive increases with the number of cigarettes. In IVF, the pregnancy rates per cycle are reduced in smokers compared with non-smokers (OR: 0.66). Menopause arrives on average 2 years earlier in the smokers, and the damage to ovarian reserves increases with smoking. The deleterious effects on the ovaries occur early in utero with regard to maternal smoking, and after puberty, on the pre-ovulatory period where toxic, vascular and mutagen effects induce inhibition of ovocyte apoptosis, promoting ovocyte aneuploidy and subsequently miscarriage. The protection of ovarian fertility is one argument more to stop early smoking." The French ovocyte stands for the English oocyte, which is the primordial cell that develops into an ovum, or egg, by division (see Oocyte, above). Apoptosis is the key biological regulatory mechanism, a programmed cell death, essential in normal development. Aneuploidy is an abnormality involving a chromosome number (one chromosome set is incomplete). The subsequent miscarriage is a case of the selection bias against abnormal human embryos – as briefly discussed under Embryo, above.

A lower mean number of oocytes in smokers than in non-smokers, and a higher rate of "abandoned" cycles along with a higher fertilization failure have all been reported in other papers, too. Some other publications had titles such as Unexplained infertility, and Smoking and involuntary sterility.

Smoking is also damaging to children's health. The health of children is worsened by exposure to second-hand smoke. A study from the Centers for Disease Control and Prevention (CDC) reports that smoking during pregnancy also increases the risk by 50 percent of having a child with mental retardation; this increased risk rises up to 85 percent among those who smoke a pack or more of cigarettes each day. The risk for Sudden Infant Death Syndrome (SIDS) increases among infants who are exposed to intra-uterine smoke and to second-hand smoke after pregnancy.

Women appear to be more susceptible to the addictive properties of nicotine and have a slower metabolic clearance of nicotine from their bodies than do men. Women appear to be more susceptible to the effects of tobacco carcinogens than men, including higher rates of lung cancer. Girls and women are significantly more likely than boys and men to feel dependent on cigarettes, and more likely to report being unable to cut down on smoking. While various smoking-cessation treatments and strategies appear to work similarly for both sexes, women may face different stressors and barriers to quitting smoking, such as greater likelihood of depression, weight control concerns, and child-care and family issues.

The desirability of developing, if at all possible, a smoking-cessation aid application of the bioZhena technology (or of any technology, for that matter!) could hardly be over-emphasized.

Sperm and semen:

Sperm is the male reproductive cell; it is the male gamete, also called the spermatozoon (plural: spermatozoa) or spermatozoid. Semen is the thick white fluid that contains spermatozoa and that is ejaculated by the male genital tract. During ejaculation, about one teaspoon of semen spurts out of the penis. Semen has a milky white colour, with the consistency of egg white. Sperm account for only about 2% to 3% of semen. Most of the semen consists of seminal fluid, i.e., the secretion of the seminal vesicles and the prostate gland, which provides a vehicle for carrying the sperm into the vagina. A normal ejaculation contains 200 to 500 million sperm. The sperm are very tiny. They are the smallest living cells in the human body - whereas the eggs are the largest. Basically, sperm are designed so that they can deliver their contents - the male genetic material - to the egg. That is why sperm are designed like projectiles - the male's DNA is found in the chromosomes in the sperm head nucleus, and the tail propels the sperm up towards the egg.

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Sperm are very fragile. Consequently, very few are able to survive the hazards of the swim through the female reproductive system in order to reach the egg. This is why a male produces such a large number of sperm. The body keeps producing sperm as long as a man has even one normal testicle. If ejaculation does not occur for many days, the sperm in the male reproductive ducts simply die. According to the American College of Obstetricians and Gynecologists, sperm retain their capacity to fertilize an egg for about 48 hours [http://www.medem.com/search/article_display.cfm?path=n:&mstr=/ZZZH6QKJ27C.html&soc=ACOG&srch_typ=NAV_SERCH]. Most other authorities put the fertilizable lifetime of sperm at more than that. Best available evidence suggests 3 days.

SPINNBARKEIT:

The somewhat archaic German gynecological word refers to the stretchability of the cervical mucus, which is generally stretchy, slippery and clear during the fertile days.

Steroid hormone:

Any hormone belonging to a group of structurally related biological compounds, based on the cholesterol molecule. The steroids control sex and growth characteristics. They are highly fat soluble, not soluble in water, and are unique in that the receptor sites of their hormone action are inside the cells in the cell nucleus (the genes), rather than on the cell membrane. They penetrate the cell membrane because the membrane is made of lipids, the fat molecules. The fat solubility gives these steroid molecules some significant attributes: Their actions and fate are under tight control of the naturally fine-tuned system of metabolic enzymes. And they are not easily made into medicinal pills because those need to be water soluble, and somehow minimally altered by the metabolic enzymes. Examples of steroid hormones are estrogen, progesterone and the androgen testosterone, all present in both sexes. The sex hormones regulate the growth and function of the reproductive organs, the development of secondary sex characteristics, and the behavior of animals and people.

Here is how the Pulitzer writer Natalie Angier relates to the steroids in the book "Woman" (page 181): "There are hundreds, if not thousands, of steroid and steroid-like hormones in nature. By definition, a steroid hormone is an elaboration of that ubiquitous and unfairly maligned molecule cholesterol. Cholesterol is a steroid in structure, but it is a no-frills steroid and not in itself a communication vehicle [meaning a hormone]. Only with chemical embellishment does it assume the mercurial role of hormone. All steroid hormones in vertebrates are built of cholesterol. … Even if you never touch cholesterol-rich food such as eggs, oil, and meat, your liver continues to make cholesterol around the clock, and with reason. Cholesterol is an essential component of the plasma membrane, the fatty, protective coat surrounding every cell. … Cholesterol is the fat of the earth and the fat of the brain. The steroid hormones, then, are pieces of ourselves, of the skin of our cells. … The word hormone wasn't coined until 1905, and the first one wasn't isolated until the late 1920s, but people have known about steroid hormones indirectly for millennia, thanks to the external nature of one particular hormone factory, the testicles. Males, including the human ones, were the hapless recipients of the first experiments in endocrinology. Game animals were castrated to make their behavior more manageable and their meat tastier. Men were castrated to render them trustworthy. The Old Testament describes the use of eunuchs to guard the consorts of Hebrew kings and princes…"

Refer to the "Woman" book for much more of the interesting history of the steroids. Including about the European "castration mania in the seventeenth and eighteenth centuries, when thousands of parents [of boys with promising soprano voices] had their sons orchiectomized in hopes of stardom and wealth" – until the "tastes and operatic singing techniques changed, and

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the diva soprano supplanted the castrato as the keeper of the angels' registers". This happened at a time when A.A. Berthold "fathered the modern science of endocrinology in the mid-nineteenth century, with a series of landmark rooster castration experiments at the University of Goettingen" in Germany. He implanted their testicles "inside the young birds' bellies, and lo, the birds matured into perfectly normal roosters". Having dissected the birds that did not become capons, he observed that "the transplanted gonads had taken root in their new position… Because the nerves to the testes had been irreparably damaged in the course of the transplantation, Berthold… correctly surmised that… some sort of substance, some eau vitale, must be traveling from the gonadal tissue through the bloodstream to other parts of the body, thus transforming cockerel into cock." As Natalie Angier puts it, "the male body gave birth to hormone research, but the female body reared it to maturity. In the 1920s, scientists began experimenting with extracts from the urine of pregnant women … and they found that something in the pee had a dramatic effect on the rat uterus and vagina… and in 1929 they isolated the world's first hormone, estrone. Estrone is an estrogen, the family of [steroid] hormones that we call female hormones, although both sexes – all sexes – have them."

Steroids are the numerous naturally occurring or synthetic fat-soluble organic compounds having all the same basic structure (of 17 carbon atoms arranged in four rings). Steroids include the adrenal and sex hormones, certain natural drugs such as the digitalis compounds active in the cardiovascular area, and the precursors of certain vitamins. They also include sterols, and bile acids, the liver-generated steroid derivatives, such as cholic acid. Sterols are steroid-based derivatives classified as alcohols. They are predominantly unsaturated solid alcohols present in the fatty tissues of animals and plants. A sterol has a hydrocarbon side-chain of 8-10 carbons at the 17-beta position and a hydroxyl group at the 3-beta position (therefore an alcohol). Cholesterol is a sterol. Because of its water soluble property at the -OH end and the fat solubility at the hydrocarbon side chain as well as the basic steroid structure, it can be incorporated into the fatty cell membranes (lipid bilayers) and interact with the water soluble substances on the outside of the membranes.

While fat soluble, the steroid structure is electrochemically active. This means a free radical activity, which can be medically either good (protective) or bad (destructive). For more insight into the chemistry of steroids, try http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/basics/steroidogenesis.html . Don't be put off by the word cyclopentanoperhydrophenanthrene ring, just view the structures and ponder Mother Nature's design features! Perhaps you now have a better feel (seeing the small structural differences) for why it should be that, as was stated in the progestogen entry (above), each progestogen (= progesterone analog) is functionally so different. Each has a different potency in terms of its progesterone effect, and in terms of the androgen side effects (such as to stimulate acne and hair growth), and/or a partial estrogenic effect. When you have pondered that, you can treat yourself to some photomicrographs of the sex hormones, which are in what the ladies - quite understandably - refer to as gorgeous colors: http://www.oxford.net/~tishy/hormonepics.html . But, is it not striking how profound are the differences between the steroids in the photos here? And, think of it, this is only the microscope - where the colorful image-forming simulates the much more sensitive molecular receptor response!

Stress:

The medical term is stress response, and it refers to the overall reaction of the organism to any adverse stimulus, whether it be of physical, mental or emotional kind, internal or external. The purpose is to adapt to challenge, and this goes on all the time. (C'est la vie! Real life is a never-ending series of stress responses.) Should the compensating reaction of the organism be inadequate or inappropriate, a pathological disorder may result. The HPA axis, the immune system and the sympathetic nervous system are involved in the stress response. It is a matter

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of conventional wisdom that perturbations in the external or internal environments (stress) can interfere with normal course of the menstrual cycle.

bioZhena is basically involved with non-pathological stress responses through monitoring certain end-organ effects. Abnormal cyclic patterns of the end-organ effects may serve as an early warning of pathological disorders. Activation of the hypothalamus-pituitary-adrenal (HPA)-axis by physical, chemical, and psychological perturbations is known to result in elevated levels of serum corticosteroid hormones. Corticosteroids are principal effectors in the stress response and are thought to be responsible for both adaptational and maladaptational response to perturbing situations. They have profound effects on mood and behavior, and affect neurochemical transmission and neuroendocrine control.

Cortisol, the predominant corticosteroid in primates, is often regarded as the "stress hormone" and consequently serves as a marker of stress. Cortisol can be measured in blood, urine, and saliva. For information about the adrenal gland and stress, go to http://arbl.cvmbs.colostate.edu/hbooks/pathphys/endocrine/adrenal/index.html .

Subfertility (THE INITIAL TARGET OF BIOZHENA):

A state of less than normal fertility but not as bad as clinical infertility. Also called reduced fertility, it refers to the inability to conceive for more than about 4 months but not more than a year (which then becomes classified as clinical infertility, the inability to conceive after a year of unprotected intercourse). It is estimated that as many as one in six couples (17%) have difficulty in conceiving the number of children they want when they want them. Again: The latest research suggests that between 14 and 17 percent of couples are affected by subfertility at some time during their reproductive lives. In fact, only eight out of 10 couples trying for a baby do get pregnant within 12 months. For approximately 10 percent of couples, pregnancy will still not have occurred after two years (clinical infertility). Sometimes the label of subfertility is used for couples who have had regular unprotected sexual intercourse for all of two years without conception taking place. This is a reflection of the fact that subfertility is becoming more and more commonplace.

According to one source (http://www.womens-health.co.uk/), even for a healthy fertile couple, the 'per month' success rate (conception rate) is only around 15-20%, "so it is not at all uncommon to take some months to conceive". Overall, around 70% of couples will have conceived by 6 months (a 30% subfertility rate). 85% conceive within 12 months (a 15% subfertility rate, "for the less impatient"). And 95% will be pregnant after 2 years of trying (technically, this is a conservatively estimated infertility rate of 5% – c.f. the 10% referenced above; or, this statistic might be perhaps considered the subfertility rate for the angelically patient). The monthly success rate in this population is 8%, and this statistic drops progressively as time goes on.

As for possible causes of difficulty to conceive, alcohol consumption, even in small amounts, can reduce a woman's chance of conceiving by more than 50 percent, and smoking "…drastically reduced fertility in our sample", as wrote a team from the Baltimore-based Health Care Financing Administration, in a report published in "Fertility and Sterility" (1998; 70: 632-637).

In terms of help, many people believe that fertility drugs, even when effective, remove conception from the intimate relationship between the partners, which means that it is to some extent beyond their control. Besides this loss of control, there are drawbacks and disadvantages to all forms of medically assisted conception. Some of them have potentially serious long-term effects. Consequently, many couples prefer to avoid these risks.

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Women who describe overcoming infertility with the help of alternative therapists went to them because they had been offered drugs to induce ovulation but were reluctant to take them, when they learned of the possible side effects. Disturbing reports have appeared about the long-term as well as short-term effects of assisted conception. Increased miscarriage levels and premature and multiple births are not only very distressing but have considerable cost implications, both personally and societally (i.e., this is a public health issue). Babies born prematurely, or in multiple births, are at a disadvantage from the start. There are also some reports of increased rates of ovarian cancer in women who have taken fertility drugs, and of cancer in the babies of mothers who have had ovulation induced by drugs.

Subfertile couples are naturally interested in methods and tools that can help them to overcome the difficulty to conceive. The endocrinologist professor Brown may be quoted: "Failing to conceive when wanted is stressful and therefore favours infertility. It should be remembered that, apart from a few conditions such as blocked fallopian tubes, absent sperm and continued anovulation, most couples will conceive eventually without help. However, the modern expectation is one of immediate results, and the main function of assisted reproduction techniques is therefore to shorten the waiting time for conception." To which we would add that bioZhena aims to offer a more affordable and safer alternative.

With the mentioned statistics of the fertile-age women suffering from the subfertility problem, this is a truly large opportunity in a constantly renewing and growing market. We are talking about 9 or 10 or even 18 million women in the USA alone – or quite possibly many more, taking into account all the impatience and demand for instant gratification in people today; plus about 50% of the 10 million of clinically infertile US couples, that is those who cannot afford the very costly ART treatments.

This is the initial, early-stage, mission of bioZhena Corporation: To provide a definitive timing aid to couples experiencing difficulties in conceiving a baby. See also the entry for the Ovulona, where it is explained that, in this situation of reduced fertility, the basic problem is the proper timing of the intercourse.

Sympto-thermal method:

An NFP method that combines the measurement of the BBT with the self-assessment of cervical mucus and cervical position, along with any other secondary signs of fertility.

T

Telemetry:

The science or process of making remote measurements and sending the data over radio frequencies (RF). The term telemetry stems from two Greek words meaning remote (telistos) and measure (metros). Telemetry is remote measurement or the remote collection of data, which can be physical, environmental or biological (biotelemetry). Telemetry is well advanced and is typically used to gather data from distant, inaccessible locations, or when data acquisition would be dangerous or difficult. Sensors measure physical quantities, and store or transmit the resulting signal. A transducer is a device that converts the output of a sensor into a useful format, typically a voltage or current, which changes proportionally to the sensor response.

A device may act as both sensor and transducer, which is the case of the bioZhena technology, whereby the tissue response to fertility status is detected as capacitive admittance (reciprocal

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of impedance). Most wireless medical telemetry equipment operates in the private land mobile radio service (PLMRS) band of frequencies, or as a secondary user in commercial broadcast VHF (very high frequency) TV bands. Very importantly, there is now FCC's new Wireless Medical Telemetry Service (WMTS) which designates specific radio frequency bands for medical telemetry in the U.S., including channel 37 (608-614 MHz) and two higher frequency bands. Because neither land-mobile radios nor television is allowed to operate on these frequencies, these bands are safe from the sources of RF interference that are common to medical telemetry. bioZhena will utilize this in its agricultural products as well as in the human parturition (birth) alarm adaptation of its technology. In due course, this could yield a very user friendly cervical cancer screen tool, and perhaps even a new generation of the Ovulona product line.

Temperature shift:

The rise in waking temperature (BBT) that divides the preovulatory low temperatures from the postovulatory high temparatures on a biphasic chart. The postovulatory temperatures are usually at least two tenths of a degree higher than those of the previous 6 days. The temperature shift rule states that the women is "safe" (will not conceive) starting in the evening of the third consecutive day her temperature has been above the coverline. The rule reflects the inherent lack of accuracy of the BBT method.

Timing (of insemination):

Although we have not yet coined a Latin or Greek word for it, many in the reproductive business will not disagree with the maxim that "timing is everything". The reason for this emphasis on "the right time" was explained under the heading Fertile phase or fertile window, and the lifetime of human sperm was discussed under Sperm and semen. Pertinent information was also summarized under Fetal sex preselection, where we stated that with the BioMeter technology, it should be possible to investigate questions such as whether different species have different lifetimes of the sperm, and to establish what kind of a distribution of sperm lifetimes there may be within a given species.

Here now is an overview of the issue of insemination timing as it pertains to several mammalian species, and as discussed by the respective reproductive specialists. The data are quoted verbatim under Bovine, Equine and Porcine, respectively, from which is extracted the following summary of gamete lifetimes in the different mammalian species.

Bovine sperm 20 –24 hours. Bovine egg 6 – 8 hours.
Equine sperm 24 – 48 hours. Equine egg 5 – 8 hours.
Porcine sperm 12 – 36 hours (10 days???). Porcine egg approx. 8 hours.
Human sperm 48 hours (85 hours??? Not likely). Human egg 12 – 24 hours. [More likely 8 or 8 – 12 hours.]

Human data from http://www.columbialabs.com/html/crinwom/infertility/fertilization.htm :
The fertilizable life of the human ova is not known exactly, but most estimates range between 12 and 24 hours after ovulation. Equally unknown is the fertilizable lifespan of the human sperm. The most common estimate is 48 hours; however, human sperm have been found in the fallopian tube as long as 85 hours after intercourse. It is not known if these sperm have retained their fertilizing ability, since motility [the ability to move] can be maintained after the sperm have lost their ability to fertilize. Recent data has made it clear that intercourse must take place before ovulation or the window of fertilization will be closed because the cervical mucus becomes hostile to sperm. [sic]

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From the above, it is not clear whether there are species differences in gamete lifetimes or whether the data reflect the lack of accuracy of existing methods of ovulation detection. It should be amply clear, however, that the need for the bioZhena technology is large and fundamental. Among other things, the bioZhena tools will make it possible to resolve the question of gamete lifetimes in a definitive manner.

As for a perspicaciously propounded scientific word for it, one may be in the offing, too: http://www.perseus.tufts.edu/cgi-bin/lexindex?lookup=kairo/s&lang=Greek kairos III. more freq. of time, exact or critical time, season, opportunity, Chronou k. Soph. El. 1292: usu. alone, k. [estin] en hôi Chronos ou polus ktl. Hp. Praec., cf. Chrysipp. Et Archig.ap.Daremberg Notices etextr. des MSS. médicaux au=Hp. [etc., etc., etc.]

Tissue:

A part of an organism consisting of an aggregate of cells having a similar structure and function. An aggregation of morphologically similar cells and associated intercellular matter acting together to perform one or more specific functions in the body. There are several basic types of animal tissue: muscle, nerve, epidermal (epithelial), and connective. Bone and blood are also tissues. Epithelium is the covering of internal and external surfaces of the body, including the lining of vessels and other cavities. Everything that enters or leaves the body must pass through an epithelium. It consists of cells joined by small amounts of cementing substances. Histology and cytology are the disciplines that study animal and plant tissues and cells. See: http://www.e-histology.net/tissues.html and http://www.rttinc.com/rtt/tmills/cytology.html . The term "tissue" is significant in the context of bioZhena Corporation's intellectual property. See also under Biosensor.

U

Ultrasound scanning:

The growth of follicles, rupture of a follicle (ovulation) and development of a corpus luteum can be visualized by ultrasound scanning. In fact, the actual rupture of the follicle, the extrusion of the ovum and follicular fluid and/or the smaller size of the ovulated follicle, can all be seen. This is thus the most accurate method of detecting ovulation. Ultrasound scanning (US), also called sonography, plays the primary role in imaging (visualizing) the female pelvis, and has played an important role in providing basic information on all phases of ovarian activity. However, for daily application, ultrasound scanning is impractical and expensive. It is therefore necessary, and usual, to assess ovarian activity and fertility status by another method, and to use ultrasound scanning as the definitive confirmation of the alternative method, in clinical studies. But even the ultrasound method is not 100% reliable because up to 20% of ruptured follicles may not ovulate (that is, release the egg). It is prudent to seek evidence corroborating that a seen ruptured follicle signifies an ovulated follicle.

It is instructive for the reader to have an idea about this "gold standard" reference technology, to appreciate the bioZhena alternative. According to a book for radiology residents (The Core Curriculum, Ultrasound by W.E. Brant, published by Lippincott Williams & Wilkins, 2001), the primary indications for female pelvic US examination are pelvic pain, abnormal vaginal bleeding and suspicion of pelvic mass. Among additional indications are infertility and early cancer detection. The US examination is routinely performed both trans-abdominally (TA) with a full bladder and trans-vaginally (TV) with the bladder empty. The TA technique is said to provide the best overview of the pelvis, but is less comfortable for the patient because of the

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full bladder requirement. For the TV examination, the bladder is empty but the patient is asked to lie supine on the examination table, with pads under her buttocks and frequently with her feet in stirrups. The textbook states that "prudence dictates that a woman should be in the room at all times during a vaginal sonogram, either as the examiner or as a chaperone." The book explains that ultrasound "requires a systematic and detailed inspection of anatomy using a small field-of-view. The mind must be connected to the hand and the hand to the eye to keep pace with the changing image as we position the transducer and visualize moving structures within the living patient."

What do we think, does it sound like a worthwhile endeavor, to aim to develop a new industry standard for fertility monitoring, when the technique that currently serves in that capacity has the attributes outlined above?

Uterus:

A hollow muscular organ located in the pelvic cavity of female mammals in which the fertilized egg implants and develops, having traveled from the ovulating ovary through the fallopian tube. The uterus lies deep in the lower abdomen - the pelvis - and is just behind the urinary bladder. The uterus is shaped like a pear and is about the size of the fist. Inside the muscular walls of the uterus is a very rich lining, called the endometrium, and it is in this lining that the fertilized egg gets implanted. If, however, pregnancy does not occur, this lining is shed along with blood in the form of the menstrual flow. Also called the womb, the uterus is connected with the vagina by a narrow passage called the cervix. For additional information, go to http://www.e-uterus.net/ .

V

Vagina:

The approximately cylindrical canal leading from the external opening of the vulva to the cervix of the uterus in female mammals. From Latin vagina, meaning the sheath or scabbard. [Note: Greek kolpos, vagina, womb – see Colposcopy.] Nature's design of this passage between the uterus and the outside world is such as to chemically protect the uterus and beyond. Only during the limited period near ovulation is the chemical protection removed, so as to allow the sperm to enter the uterus through the cervix. At all other times, the acidity of the vagina, and the thick hostile mucus blocking the cervix, prevent any microorganism – including the sperm - from penetrating into the uterus and beyond. Here is how it works.

The healthy vaginal fluid is acidic, with a pH of 3.8 to 4.5. That is somewhat more acidic than black coffee (with a pH of 5) but less piquant than a lemon (pH 2). In fact, the acidity of the robust vagina is just about that of a glass of red wine. The healthy vagina is also full of germs, good germs, called lactobacilli, which are the same bacteria as those found in yogurt. The moisture, and the proteins and sugars of the vaginal tissues maintain a stable population of lactobacilli, which keeps competing bad bacteria out. The good "lactos" generate lactic acid and hydrogen peroxide, which are disinfectants that prevent colonization by less benign microorganisms. It is ironic or perhaps somewhat counter-intuitive that by douching women can make themselves dirtier than ever. Douching kills off the beneficial lactobacilli and paves the way for infestation by other microbes and particularly some anaerobic bacteria (living in absence of oxygen). It is the anaerobes which, when they proliferate, secrete foul-smelling compounds such as trimethylamine and putrescine, the compounds found in putrifying fish and meat. This is even worse in the case of bacterial vaginosis, a condition that can arise in the

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wake of other infections, such as pelvic inflammatory disease. Women with bacterial vaginosis are more susceptible to gonorrhea, syphilis, and AIDS.

Some women are born with an unfortunate predisposition toward imbalances of vaginal flora, just as some are susceptible to acne. But then, even the desirable and inherent lactobacilli vary in terms of their potency, with some strains more able than others to generate hydrogen peroxide, and thus more efficient at fending off the contending foreign microorganisms. Women with the less potent "lactos" are more susceptible to vaginosis, as well as to infection by yeast, which is another type of microbe that thrives in highly anaerobic conditions (absence of atmospheric oxygen). These women can try to rectify the imbalance by eating a lot of yogurt, but especially chronic vaginosis requires a treatment with antibiotiotics; a topical delivery via a suppository is better than a systemic intake.

Interestingly, frequent intercourse can also cause a problem because semen is highly alkaline, with a pH of 8 (more alkaline than any other body fluid, including not only spit but also blood, sweat and tears). This is so (designed by Nature) because sperm cannot swim in the acidic environment of the healthy vagina. For several hours after intercourse, the overall pH of the vagina rises, thus momentarily giving the exogeneous microbes the edge. Usually the change is fleeting, and the woman's body has no trouble readjusting the pH of the vaginal fluids back to status quo. The restoration is particularly easy when the sperm looks familiar – that is, when it belongs to the woman's regular partner. Upon exposure to the semen of multiple partners, the homeostatic mechanism sometimes falters, probably due to some immunological reaction to all that strange sperm. Just when the acidic protection against disease would be needed the most, the vaginal ecosystem is too alkaline…

W

Waking temperature:

The same as the BBT, basal body temperature, which is the temperature of the body at rest, taken immediately upon awakening, before any activity. The hormone progesterone is responsible for the post-ovulation rise in the BBT, but the BBT also responds to other stimuli that cause false temperature rises, such as fever, restless sleep, or drinking alcohol the evening before, or antidepressant medications. There is nothing in the bioZhena technique that would correspond to the waking aspect of the BBT. We simply advocate that the measurements be performed at about the same time of day, any convenient time of day, give or take an hour.

X

Xeno-estrogens:

Xeno-estrogens are chemical contaminants introduced into the body from the environment. They mimic the action of estrogen produced in cells and thereby alter hormonal activity. Exposure to these compounds is responsible for many reproductive problems in humans and animals. They are also being related to breast cancer and testis cancer. Some naturally occurring and easily degraded xeno-estrogens, such as those found in soy products, cabbage, broccoli and cauliflower, can reduce estrogen effects. Others, usually synthetic and difficult to degrade, amplify estrogen effects, causing dangerous proliferation of cells.

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For more information about these endocrine or hormone disruptors, go to http://www.tmc.tulane.edu/ecme/eehome/sources/links/envirohorm.html .

Z

Zygote:

The fertilized ovum (egg), a single fertilized cell resulting from fusion of the sperm and egg. The name is given to the structure created when a male and a female gamete have merged but before it begins to multiply. After further cell division, the zygote becomes an embryo. The zygote intra-fallopian transfer (ZIFT) is one of the assisted reproductive technologies (ART), in which a woman's egg is fertilized by her partner's sperm in a petri dish and the resulting zygote is then placed back in her fallopian tube.

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