

# **Advanced Maternal Age and Egg Quality**

Randine Lewis, Ph.D., Lic.Ac.

#### Biologic Age vs. Chronologic Age

Many humans live over 100 years. Most forms of medicine throughout history have sought to improve longevity. In the ancient Chinese medical text, the Nei Jing, there is a dialogue between the Yellow Emperor and an old Taoist teacher named Chi-Po. The Yellow Emperor asks, "Why does medicine exist?" Chi-Po's answer is, "...because people have severed themselves from their roots (the Tao)". Reconnecting a woman with her spiritual roots is an important aspect in maintaining her health and her youth. Understanding which energies decline with maturation can help restore youthful energetics and, in essence, turn back the reproductive clock. One's longevity is deeply connected with one's inner harmony. The result is manifested internally and externally. Nature is kind forgiving. Enhancing our natural reproductive capacity will maximize the possibility of a child; however, we cannot wait too long and override nature. According to an old Chinese proverb, "The Yangze never runs backwards... man recaptures not his youth."

The average reproductive life span for a woman is about 30 years. Years ago, women didn't menstruate on the average until age 15 or 16. Today girls of 10 or 11 are already menstruating. Part of this is due to the overabundance of synthetic hormones in our diet. We are coming of age faster and going into menopause later. We should be able to prolong our reproductive health as well as longevity.

Specifically applied techniques of Oriental Medicine can restore a more youthful endocrine system. Correct dietary practices and exercise routines are the first factors to contemplate in raising your fertility quotient and maintaining reproductive vigor. R.G. Godsen & C.E. Finch, in Definition & Character of Reproductive Aging & Senescence, state, "Dietary and endocrine manipulations can also slow the pace of ovarian aging." One study in Biol Reprod, 1985, Nelsen, Godsen & Felicio, found that feeding a low calorie diet to rodents slowed the disappearance of ovarian follicles. Whole foods, mainly consisting of organic fruits and vegetables, will help restore vitality, as well as avoiding alcohol, caffeine, and nicotine. Moderate tobacco use has been estimated to advance the onset of menopause by up to three years, and increase the rate of follicular atresia by 7% (Godsen, et al.) Any form of stimulant (including herbal) will age us prematurely. Moderate exercise at least three times per week helps improve the circulation to the internal organs as well as improving skin and musculoskeletal tone

There is a belief in the reproductive medical community that age is the only factor that determines ovarian health. Medical studies conclude that ovarian decline occurs around age 40. These studies, however, do not take into account the relevance of environmental stressors and dietary factors. Environmental factors play an incredibly crucial role as far as reproductive aging is concerned. In 20% of monozygotic twins, the age at menopause differs by five or more years. Genetic parameters of oocyte aging have used mathematical models to calculate and determine that an 80% variation in ovarian aging is genetically determined, leaving a 20% distinction for environmental factors which are within our control. Guess what?! Our ovaries do not have a predetermined, finite half-life. They are organs that respond to favorable surroundings just as the rest of our bodily systems do. They are not locked away in untouchable safes. This is very good news, however, because just as they respond negatively to poor diet, drugs, toxins, and stress hormones, they also respond positively to a healthy diet and pure lifestyle.

Our ovaries and the eggs residing in them have been present since before we were born. During embryologic development, the seven million germ cells which will become all of the 300,000 - 400,000 eggs we will possess at birth will be carried through menopause, when the follicular supply falls to less than 100. Certainly as we age, the DNA contained within the eggs becomes less stable. However, a human egg which has been lying dormant for 32 years is not itself tremendously more stable than one which has been resting for 40 years. When most women aproach the peri-menopausal hormonal fluctuations, they still have thoudands of eggs remaining within their ovaries! What makes them less

responsive? Hormonal fluctuations. Once scientific study found that when the ovaries of older, anovulatory rats were transplanted into hormonally youthful rats' bodies, they became capable of ovulating. Neuroendocrine changes take place while the ovary is still well endowed with follicles. These variations begin with central, hypothalamic control of the release of FSH. Acupuncture and herbal therapy can forestall age related decline.

What happens as we approach middle age is that our own hormonal makeup wavers. The hypothalamic - pituitary - ovarian axis, an invisible network of hormonal relationships which govern our reproductive status, becomes less stable with age. The ovaries become less predictable because of the hormonal fluctuations and the eggs contained within quit responding predictably to the hormones. Once they become less responsive to the FSH, more of them cycle through and go to their "resting place." We need to provide more hormonal fuel for the remaining thousands of eggs, i.e., strengthen the hypothalamic-pituitary-ovarian axis, when age becomes an issue. Acupuncture techniques have been proven to regulate the hypothalamic - pituitary - ovarian axis. The result will then be manifest in the ovaries and their hormone production.

Contrary to popular reproductive belief, follicular growth from the resting state until ovulation takes up to 100 days, or more than three menstrual cycles. Follicles are selected from the primordial pool of resting follicles almost a year before ovulation, and are recruited to become active. During the initial pre-gonadotropin period the follicle responds to regulatory factors within the ovary itself, which are like hormones. These growth factors are like hormonal precursors. One important ovarian growth factor, insulin-like growth factor, is the precursor to the youth hormone which is secreted by the thymus gland called growth hormone. Others have names like insulin-like growth factor binding protein, interlukin, tumor necrosis factor, inhibin, vascular endothelial growth factor, and activin. These ovarian growth factors help determine the eventual fertility potential of the oocyte (egg).

During this period which lasts for many months, the healthy, responsive follicle determines its own fate with these regulatory proteins. The (0.03mm) follicle is first chosen from the primordial pool to double in size (to about 0.06 mm) and become a primary follicle, about 150 days prior to ovulation. It reaches its secondary phase approximately 120 days before ovulation, when it again doubles in size. The follicle then cycles through the pre-antral and early antral phase and grows from about 0.12 mm to about 1.0 mm in approximately 65 days. It has quadrupled in size during this time, and has gone through many stages of proliferation.

It is only during the last two to three weeks of its cycle through the ovary that the follicle becomes dominant and responsive to FSH. During the selection phase, which lasts approximately ten days, it more than doubles in size as it differentiates further. The follicle itself acts as its own gland by autocrine and paracrine mechanisms to make itself responsive to FSH. Now the follicle grows to twice its previous size again, surfaces and becomes the estrogen-producing follicle which then makes itself receptive to luteinizing hormone by expressing a receptor at the preovulatory phase. It fulfills its major purpose as it releases its egg, whose chromosomes are beginning to rearrange, for a chance to become fertilized. The follicle then finalizes its life cycle by becoming its own endocrine gland called the corpus luteum, which secretes progesterone to maintain a pregnancy. Imagine the potential energy required for these great follicular achievements! This is not an undertaking for the frail!

A woman who is over age 43 or 44 will often be turned away from any chance at assisted reproductive technology because of the age and therefore poor state of her ovaries. She may fail to respond as favorably to the gonadotropins as her younger counterpart, because her eggs have become less responsive to hormonal stimulation. She may produce few numbers of eggs, whose outer capsule is tougher and thus less capable of fertilization. Those eggs which do become fertilized may have more inclusions during early embryologic development, meaning there are more waste products put out by the mitochondria. Less make it to the blastocyst stage, even fewer are capable of implantation, and fewer yet make it through the full embryonic development. That is why a woman over forty is statistically less likely to give birth, and is encouraged to find alternative ways of becoming a mother. She will be told she has poor quality eggs. Her reproductive endocrinologist will strongly suggest that she consider using a younger donor's eggs. This makes her chances of having a baby, and thus her RE's statistics, much higher.

The reason for the lower chances of assisted reproductive success in older women is because the only portion of the hormonal process that is manipulated is the last few weeks of this many months' process. Massive doses of gonadotropin hormones are given to the women in order to (hopefully) recruit more follicles. This doesn't, however, make them of better quality. Perhaps the reason she has been unsuccessful in conceiving in the first place is because her hypothalamic-pituitary-ovarian axis has been ailing, and the reflection has been in the resistance of her ovaries, the eggs contained within, and thus the inability to conceive.

It seems that the older a woman is, this process of follicular development, which takes up the better part of a year, becomes more susceptible to breakdown. Experience has shown that if the hormonal system is in perfect working order and a woman has clockwork menstrual cycles, no matter what her age, a healthy egg can be released on time. It then has a good chance of becoming fertilized, implanting, and making it through embryologic development to become a child. The emphasis here is on the healthy hormonal cycle. If each individual element of the hypothalamic-pituitary-ovarian axis is still in healthy interrelationship dring this process, the developing follicles are going to reflect this state of well-being.

How do we give the HPO axis the attention it needs to express its full reproductive vigor? Fortunately, the steps involved in turning back the reproductive clock are all natural. Unfortunately, rejuvinating the reproductive system takes time. Through some effort, we will give the entire reproductive-psychoneuro-endocrinologic system the attention that a young woman's has effortlessly. We will help urge the body's attention to the mid-brain, the pituitary, the ovaries, the uterus, the spirit, and the mental and emotional health required to produce healthy eggs.

#### The Eastern View

Three energy meridians make up the hypothalamic-pituitary-ovarian axis: the Penetrating, the Conception, and the Governing meridians. These energies become fulfilled when a girl reaches menarche, and become depleted when a woman enters menopause. Statistically, the earlier a young woman first menstruates, the later will be her entrance into menopause. Her reproductive age span is a function of her underlying congenital source qi.

The Penetrating meridian represents the HPO axis. It originates in the uterus and presides over the function of menstruation and governs the hormonal cycles. It is the deepest level of life, which equates with the most innate functions of our more primitive brain, as it relates to the psycho-neuro-endocrinological system. From it arise the energies of the conception and governing meridians, the yin and the yang of the endocrine system.

The inherent functions of these meridians are the basic forces of our internal nature which determine cellular health, cellular division, continued development, maturity and decline. We might say that the Penetrating meridian is responsible for the follicular manifestation of growth factors and hormonal expression.

We all have been programmed with a certain reproductive energetic potential which governs hormonal fluctuations and eventual decline. This is not fixed. It is subject to certain environmental and internal factors which can stave off or facilitate the decline.

The usual process of reproductive transition from a fertile to a non-fertile state spans many years. It should be a smooth evolution from an energetic focus on self (pre-puberty), to an energetic focus on reproduction (menarche), to an eventual outward energetic shift (menopause). This transition is physiological, psychic, and spiritual.

The physical ramifications of these shifting energies begins when a girl enters menarche. At about age 14, the hormonal system is effulgent, and the Penetrating meridian fills to overflowing, after which the menses arrive like a tide. The uterus fills to overflowing from one full moon to the next. This process occurs every month unless a pregnancy (or other hormonal interruption) suspends the process, until the woman approaches middle age.

When her reproductive life span is complete, the energies are transferred from the uterus to the heart via the Penetrating and Conception meridians. She moves from a state of procreation (represented by the kidney system) to a state of wisdom, represented by the heart. This is seen as a literal shifting of energies. If this energetic transition from the uterus upward to the heart is not smooth, these rising energies will produce heat signs like hot flashes and night sweats. Irritability will result from the obstructed flow of qi. The kidney system will become depleted and will no longer be able to support bone growth.

When we treat menopause with Traditional Chinese Medicine, we make this transition smooth and complete. When we treat age related fertility factors, we interrupt and stall this transition. Again, we try to regulate the hormones and make them function as if they are young again. The extraordinary meridians that govern endocrine relationships cannot be separated from the kidney system.

#### The Kidney System

The signs and symptoms of declining kidney function parallel an actual decline in hormone levels.

In Chinese medicine the kidney system is responsible for our genetic constitution, and underlies all other metabolic processes. It dictates growth and development. It provides the essence for the uterus and menstruation. When the kidney essence is depleted, women go into menopause. The kidneys are responsible for bone and teeth formation and overall brain function. The kidneys control water balance and elimination.

The kidney system provides the substrate for and encompasses the relationship between the reproductive system, the skeletal system, the neurological system and the endocrine system.

When the kidney system begins to decline as a woman ages, symptoms include either signs of kidney yin vacuity, kidney yang vacuity, or both. Signs and symptoms of kidney yin vacuity are: low levels of estrogen, night sweats, hot flashes, vaginal dryness, low back weakness, soreness, or pain, or knee problems, ringing in the ears, dizziness, scanty fertile cervical mucus, excessive fear, dark circles around the eyes, scanty menstruation, a tongue lacking in coating that appears shiny or peeled.

Symptoms of kidney yang vacuity include have low back pain which is worse premenstrually, a sore or weak low back, cold feet at night, being cold in nature, low libido, frequent, dilute or nighttime urination, being fearful in nature, early morning loose, urgent stools, profuse vaginal discharge, dull menstrual blood, cold cramps during the period that respond to a heating pad, and a moist, pale tongue.

#### **Spleen Vacuity**

The spleen energies weaken with age right along with the kidneys, and often times precede it. The first tipoff to declining spleen function is fatigue. We just seem to require more energy to get the same amount of work done than we did a few years ago. Enter caffeine, which artificially stimulates the brain, and allows us to function with a little more energy. However, caffeine itself provides no additional energy to the body... it merely borrows it from... (you guessed it), the kidneys! When the kidneys are already taxed, and still have to preside over menstruation and hormonal functioning, guess what gives? Reproduction: that life process which is not necessary for our survival.

Another sign of waning spleen energies is that things start to fall. Our skin begins to sag, our breasts fall, veins appear on the surface of our skin, we get hemorrhoids, and our uterus falls into our bladder. We have to pee more often. Our blood pressure fluctuates. Our digestion and elimination become more sensitive. Our metabolism changes. We react more to our environment and catch cold more often. Even our protective mechanisms start to falter.

Progesterone drops off during the luteal phase. Periods come earlier and are often accompanied by loose stools.

## **Treatment**

Happily, we have methods to tonify both the energies of the spleen and the kidney.

- Exercise
- Rest well
- Avoid junk food, caffeine, tobacco, sodas, sweeteners, and refined carbohydrates.
- Do not eat any meat or animal products which have been treated with growth hormone. This includes most of the meat, eggs, milk products and cheese found at the supermarket.
- Avoid dairy products, raw vegetables, and cold foods.
- Eat foods which tonify the kidney and spleen, and supplement your diet with blue-green algae, wheat grass, and green power foods.

### **Kidney Vacuity**

If you suffer from signs of kidney vacuity, the following foods are found helpful:

black beans and legumes, kelp, parsley, tofu, raspberries, walnuts, wild rice, spirulina, wheat germ, wheat grass, string beans, mulberry, millet and (non-hormonally treated) organ meats, oysters, clams, lobster, crayfish, pork, venison, chestnuts, black sesame seeds, lycium fruit, aduki beans, yams, gelatin, chestnuts and corn. Glandular supplements (including placenta) also fall under this category.

Yin Deficiency (hot flashes, night sweats, vaginal dryness, lack of fertile, cervical mucus)

A diagnosis which includes kidney yin deficiency should be rich in the following foods:

- Wheat and wheat germ, tofu, millet, barley, rice, amaranth
- Black beans, kidney beans, string beans, mung beens, and bean sprouts, Seaweed, chlorella, spirulina
- Fruit like apples, bananas, raspberries, blackberries, grapes, mulberries and melons
- Eat shellfish like clams and muscles, eggs, jellyfish, organ meats like kidneys, brains and hearts (all from organic, non-hormonally treated sources)
- Avoid the use of dry, pungent, acrid spices

Yang Deficiency (pre-menstrual low back pain, low libido, nighttime urination, cold feet)

- Eat warm foods
- Include ginger root, black beans, aduki beans, lentils
- Include grains like oats, spelt, sweet brown rice, and quinoa
- Fruits should include citrus peel, dates, and cherries
- Vegetables which are yang in nature include parsnips, parsley, mustard greens, winter squash, cabbage, kale, onion, leek, chive, garlic, and scallion
- Cook with peppers and warming spices and herbs such as anise, ginger, cinnamon, cloves, fennel, basil, rosemary, dill, anise, caraway, and cumin

#### **Spleen Vacuity**

- Consume mostly organic vegetables, sauteed or lightly cooked
- Do not eat raw, cold, foods. Don't consume ice cold beverages, or ice cream and popsicles.

  Energetically cold foods should be eaten only in moderation. These include many fruits like mango, watermellon, pears, and persimmons. "Cold" vegetables include cucumbers, lettuce, celery, spinach and the like.
- Do not eat refined carbohydrates like white bread, or pasta. Avoid any food made with white flour.
- Grains like rice, Job's tears barley (coix) and sorghum supplement the spleen. Eat yams, pumpkin and pumpkin seeds.
- Avoid sugar and sugar substitutes or any concentrated sweets including honey and maple syrup.
- Avoid damp creating foods like milk and milk products such as cheese or ice cream.

The typical Chinese diet incorporates these principles. Very little cold, raw foods are eaten, very little breads or pastries, and almost no dairy products.

Herbs which help nourish the spleen and kidneys, (and, when taken for the correctly diagnosed pattern discrimination can lower FSH levels) are Astragalus, Ginseng, Chasteberry, False Unicorn, Vitex, Angelica, Epimedium, Dipsacas, Atractylodes, Dioscorea, Eucommia, Codonopsis, Rubus, Cuscuta, and Cornus. [NOTE: Do NOT take herbs if you are undergoing a hormonally stimulated cycle for any assisted reproductive technique without your primary physicians specific consent and approval.]

Co-Enzyme Q10 is a supplement which is commonly used for cardiovascular disorders. Co-Enzyme Q10 helps support and improve mitochondrial function, which is the powerhouse of the cell. Recent experimental medical techniques have been studied whereby the embryologist uses a younger woman's cytoplasm to support the older woman's DNA in IVF techniques for older women. This procedure has been banned by the FDA, but the objective of this technique was to improve mitochondrial function. A milder, but probably less potent attempt to perform the same improvement in cellular function is to supplement with enzymes like Co-Q10. Reactive oxygen species are continuously generated throughout metabolic processes which damage mitochondrial DNA, and contribute to the "age-related" decline in egg quality. Anti-oxidants (vitamins C, E, A, zinc, & selenium) and super anti-oxidants (pycnogenol) help prevent oxidative mitochondrial damage. Improved

longevity in more advanced species have evolved because of a higher intrinsic capacity for repair and stress resistance at the cellular level. We can extrapolate this into improved ovarian longevity as well. We know this can be affected by improving our environment, exercising, reducing stressors, eating a more organic, whole food diet, and supplementing with appropriate nutritional and herbal administration. These factors are within our control!

Many women are also using Human Growth Hormone analogues like Insulin-like Growth Factor, a precursor to Growth Hormone (which naturally declines with age), to improve the quality and quantity of their egg production. Some companies are manufacturing products which are touted to encourage your pituitary gland to produce more Human Growth Hormone through amino acids like L-Arginine, Glycine, L-Ornithine HCl, L-Glutamine, and L-Lysine, and Bovine Colostrum. Human Growth Hormone is not available as a supplement; the molecule is not utilizable orally. In the United States, Human Growth Hormone is available by prescription only as Somatropin, and is prescribed for growth hormone failure in children, and for hormone deficiency in adults. Some studies have shown that DHEA can be used instead of Growth Hormone to help ovarian response. A study published in Human Reproduction, 2000, reported that DHEA administration of 80 mg./day for two months improved response to ovarian stimulation after controlling for gonadotrophin dose.

One study, published in Human Reproduction, 1999, found that there was an increased ovarian response, endometrial receptivity, and pregnancy rates in IVF patients who supplemented daily with large doses (16 grams) of oral L-arginine, an amino acid.

#### OTHER REPRODUCTIVE ENHANCEMENTS:

#### Femoral Massage (Increases blood flow to the pelvic organs)

Compress the large femoral artery, whose pulse you can feel just beneath the crease between your thigh and lower abdomen. When the flow has ceased and you feel the pulsation end at your finger tips, hold for 30 seconds. Repeat on the opposite side. Perform the femoral massage three times on each side, twice daily if possible. [NOTE: Do not perform this exercise if you have high blood pressure, heart problems, any vasculature impairment, glaucoma, or have had a history of strokes or transient ischemic attacks.]

#### Qi Gong Meditation with vizualization for age related issues

This exercise utilizes the basic life force - the breath, for relaxation, and enhances the body's focus on the reproductive organs. We literally breathe life into and through the reproductive organs.

Lay on your back, with your eyes closed. Relax and breathe deeply. Notice any areas of tension you feel in your body from your head to your neck, down your arms and hands, through your torso, down your abdomen, buttocks, thighs, calves and feet. Tense the tight areas in your body even more, one by one. Breathe in, inhaling deeply down into your lower abdomen. Push your stomach out as you breathe in. Focus your attention on the tension in your body, then tighten the muscles in the area even more, and relax them fully as your exhale. Exhale all the way, deflating your abdomen when you breathe out. Breathe the tension in your body out through the breath.

Focus your attention on the tension, the breath, and the relaxation. Nothing more. When the tension in that particular part of your body is gone, move on to the next part. When you feel relaxed throughout your body, and your mind is clear, begin the visualization. Continue the deep breathing exercise, breathing deep into your abdomen and relaxing with each exhalation.

Visualize light entering your body through the top of your head with each inhalation. This light is clean and pure and represents the energy of life and youth. Breathe this light energy from the top of your head and let it pass through the base of your brain, the hypothalamus, which governs our basic reproductive functions. See this healing light enter the pituitary gland which is located behind the center of your eyebrows. Still on inhalation bring the focus of the breath down the midline of your body, between the breasts, down the abdomen, and eventually focusing your breath down to the region two inches below your navel. This is called the Dan Tien, where our life source begins. Let the breath energy pool here.

At the end of inhalation, bring the focus of light and breath from the area below your navel down to the out to your ovaries, just inside your hip bones. Let the light flow from the ovaries down the fallopian tubes and into the uterus, cleansing them of all impurities, and restoring their youthful vigor. When your uterus has bathed in the purity, turn your attention down to the perineal muscles and perform a kegel exercise, squeezing the perineal muscles to retain the light. When you release the kegel, begin exhalation.

During exhalation, Return the light with the exhalation up the midline and back through the pituitary gland behind the center of your eyebrows, and through the base of the brain, and back to the top of the head. Repeat from inhalation until the movements become smooth and continuous.

## **Barbara's Baby**

Barbara had been 42 for eight months when she first consulted me. She was single and had her own business that took her out of the country each month. Although she didn't have a partner, she knew she wanted a child, and her age was not going to provide her the luxury of finding the right father. She had been having intrauterine inseminations with frozen sperm purchased from a sperm bank every month, but would start to spot about a week after ovulation. She had a "thyroid imbalance", and was currently taking the synthetic thyroid hormone, Synthroid. The reproductive clinic also prescribed progesterone suppositories for her to take after the inseminations, but it did not curtail the bleeding. They had previously done three cycles of Clomid stimulation, but her response did not change.

She put herself in my care with complete trust. Barbara's diet was already healthy. She had been reading up on nutritional health, and had consulted a nutritionist for supplementation.

She had a presentation consistent with spleen qi vacuity. She was tired most of the time, was beginning to get varicose veins, bruised easily, and had low blood pressure. Her menstrual flow started out light pink in color and was rather watery in consistency. The flow became very heavy and lasted about seven days. We began weekly treatments of acupuncture and she took herbal formulas to supplement her spleen qi religiously. She decided not to resume inseminations until she could hold a luteal phase. She began monitoring her basal body temperatures so we could assess her hormonal status. Her chart proved somewhat erratic. She ovulated later than usual, and had a short luteal phase with a chaotic pattern. After about two months her luteal phase lengthened, but she was still spotting. She also reported that each month just before she got her period, she got a nosebleed. Once again this confirmed the diagnosis of deficient spleen qi, which was unable to hold the blood in its proper place.

Barbara began to feel like the Synthroid was doing her more harm than good, and quit taking it (after consulting her internist.) She did continue taking the herbs, and within six weeks her thyroid studies proved within normal limits. Her energy was much better than it had been previously, and her menstruation was becoming less profuse. She turned 43 and became anxious again about her biological clock. She began the monthly inseminations again, even though her spotting and nosebleeds were still present. Her temperature charts were improving, though. She was ovulating on day 15 or 16 of her cycle, and was having 29 to 30 day cycles. The luteal phase was adequate in length, but she would still get a dip in temperatures when she spotted. After three more months, (which were agonizing for her), the nosebleeds and spotting were gone.

The next month was the magical one. About twelve days after her insemination, she said she knew she wasn't pregnant because her breasts weren't tender, and she just didn't feel like it was successful this month, either. I felt her pulse, which had taken on the lively, vibrant quality of pregnancy, and assured her she had succeeded.

Barbara carried her baby girl to term, which was born soon after she turned 44. They make a great team!