

Practical Approach to Male Infertility

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Male factor infertility is present in approximately 40% of couples having difficulty to conceive. In most cases, however, it is seldom one factor. A basic element that is encountered in every case is the number and quality of eggs. Other factors in also include sexual factor and other female factors (e.g blocked fallopian tubes). Hence, evaluation of female factors is integral to evaluation and successful treatment of male factor.

Evaluation of female factors includes testing for [ovarian reserve](#) and testing of the fallopian tubes for patency. In addition to evaluation of medical, obstetric and genetic risks of getting pregnant.

Evaluation of Male Factor

Reproductive ability in males is initially evaluated through i. Detailed history of male partner and ii. sperm analysis. History can indicate many factors that may reduce the ability to conceive: social habits, erectile dysfunction, childhood infections (mumps), medical disorders, genetic diseases (chromosomal abnormalities, specific genetic diseases as cystic fibrosis), occupational exposure..etc. Unfortunately in the majority of cases history may not predict abnormalities in male factor

Sperm Analysis

Accurate interpretation of [sperm analysis](#) (volume,

concentration, movement and shape) is the most important step in evaluation. It is important to take in consideration each factor separately and then in combination. Normal parameters are volume >2mL, concentration 15million/mL, motility 40% and normal shape 4% using strict morphological criteria (Kruger).

Repeat sperm analysis is commonly recommended when abnormalities are detected. There is no strong evidence to repeating the sperm analysis. If the sperm analysis is to be repeated this should be done at least 2 months later as it would take that long for new sperm to be 'manufactured'.

Generally 10 million moving sperm per ejaculate (volume x concentration x % motility) is required for successful reproduction with intercourse and IUI. Approximately 2 million motile sperm are adequate for IVF. Lower parameters especially if low morphology <2% require IVF with intracytoplasmic sperm morphology (ICSI).

Other Tests

Genetic screening for chromosome analysis and Y chromosome micro-deletion is required in low sperm concentration (<10 million /mL) and [azospermia](#) is required. Abnormalities are found in 5-10% of men and can be transmitted to children. Genetic screening for cystic fibrosis and its congenital absence of the vas deferens is also required if azospermia (obstructive) is present.

Other sperm tests as pH, fructose and sometimes hormone analysis are sometimes helpful.

Tests for sperm DNA fragmentation is still being evaluated but are not part of routine fertility workup.

Treatment of Male factor Infertility

Improvement in sperm analysis is not the main aim of treatment. The main aim is conception and delivery of a

healthy child. Sperm analysis improvement is a surrogate outcome not a final goal. In most cases, the improvement in sperm parameters (count, movement and shape) does not translate into a higher chance for conception. In addition, in the majority of cases there is no specific cause identified for male factor abnormalities. The two practical strategies left are to wait (within what is allowed by female ovarian reserve) for sperm analysis to improve and conception to occur or to use the small / abnormal sperm available for assisted reproduction (ICSI) which is a very efficient strategy.

Four Important Considerations before Treating Male Infertility

a. Female age and ovarian reserve: any treatment for male factor should be guided with the number of eggs in the ovary and their quality (age related). In women with low egg reserve and 35 or older consideration to ovarian stimulation (to increase mature egg production) followed by IUI or ICSI should be exercised.

b. Sperm Freezing: In men with moderate to severe male factor one should consider freezing one or more sperm samples. The future sperm parameters cannot be predicted and can deteriorate even to a complete absence of sperm in ejaculates. Sperm freezing is cheap, non invasive and can save men from the need for surgical retrieval of sperm. Men undergoing vasectomy can also consider sperm freezing, prior to procedure, in case they decide to father children in the future

c. Genetic screening: there are two main values to screening males with moderate to severe sperm abnormalities to chromosomes, Y micro-deletion and cystic fibrosis. To avoid transmission to children and to counsel the couple about the chance of successful surgical sperm retrieval (TESE). In some cases the chance for finding sperm is extremely low that TESE is not indicated.

b. Urological consultation: After female and initial male evaluation is complete, evaluation by a male urologist is very useful. A urologist well versed in male infertility can counsel the couple about the chance for success of surgical sperm retrieval and following correct of obstruction.

Four Treatment Options to Consider

Surgical sperm retrieval: in obstructive and non-obstructive azospermia sperm can be retrieved directly from the testes by a male urologist. Micro-TESE involves dissecting one or both testes and obtaining multiple tiny biopsies from many areas. In real time each biopsy is examined under a microscope. The process is repeated till sperm are obtained. The best chance

Surgical treatment for obstructive azospermia: in men that underwent vasectomy before vasectomy reversal can, if successful, restore fertility. Other areas of obstruction can also be restored by urological surgery.

IUI: in few cases of mild male infertility (producing close to 10 million motile sperm) or mild shape abnormalities, ovarian stimulation and IUI is an option for 3 cycles. IUI using donor sperm is also an option.

IVF-ICSI: assisted reproductive technology is very robust and can address the majority of male infertility: low sperm count, low motility, abnormal sperm shape, prior fertilization failure. Its is very efficient that it can achieve a conception with very few available fresh or frozen sperm. It can be synchronized with surgical sperm retrieval so that fresh sperm are used for ICSI. Once sperm are available, the success of IVF is dependent on female age and ovarian reserve.

Interventions to Avoid or Consider Cautiously

Surgical treatment of varicocele: Varicocele is a common finding in infertile males and can be associated with low concentration and motility and higher abnormal shape of sperm.

Varicocele surgery does improve sperm parameters. The problem with varicocele surgery is that it is not proven to increase the odds of delivering a child by female partner. Varicocele surgery should be cautiously considered due to lack of solid evidence of its benefits.

Medical treatment: The use of medications (e.g clomid, nolvadex, anastrozole) should be avoided as there is no evidence that they will improve the chance of pregnancy and improvement in sperm parameters. The use of injection medications should only be employed in men with a specific indications related to deficiency of such hormones

Supplements: so far there is NO supplement or 'vitamin' proven to increase the chance for successful reproduction in male with sperm abnormalities.

A practical approach to male infertility requires initial evaluation of sperm analysis, ovarian reserve and genetic risk factors followed by a treatment plan oriented with the ultimate goal: conceiving healthy child not intermediate issues as cause of male infertility and improving sperm analysis.

Egg Reserve and Infertility

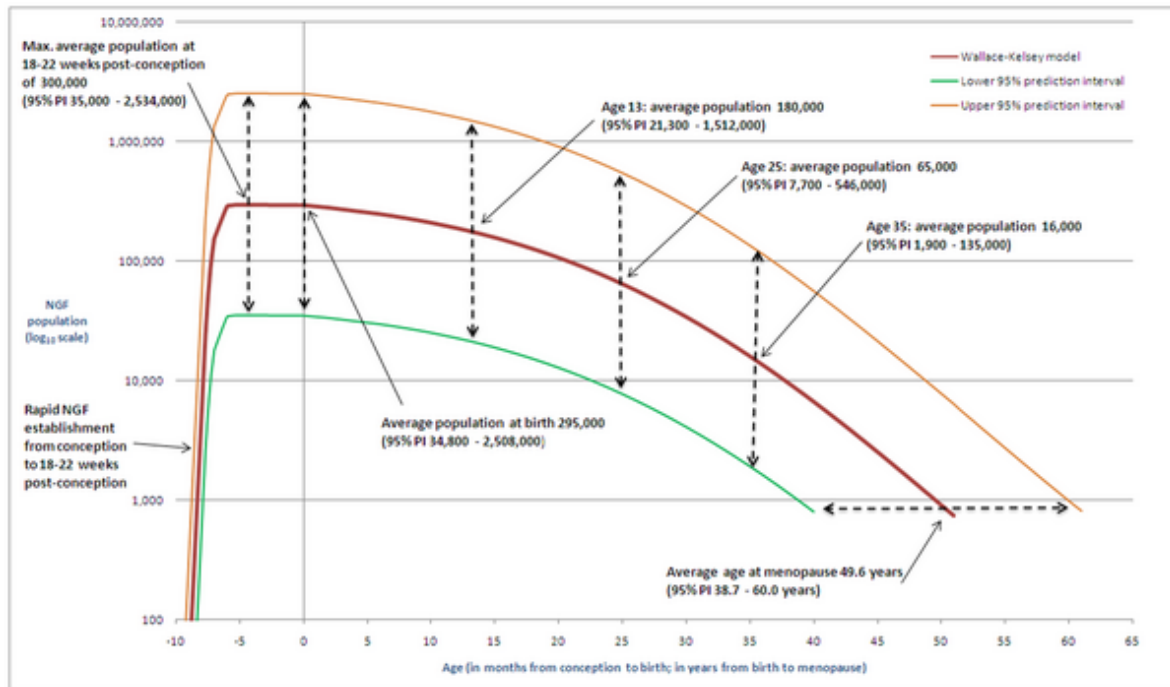
Egg reserve means the number and quality of eggs remaining in the ovaries at a given age. It reflects the fertility potential of a woman irrespective of the cause of infertility, even male factor.

Benefits of Testing for Egg Reserve

Testing for egg reserve results should be interpreted with caution. Abnormal values should not be a cause for denying fertility treatment because the predictive power for pregnancy with own eggs is modest. For women, ovarian reserve tests give women insight into the chance of pregnancy with their own eggs. It also may indicate the need to promptly avoid delay in seeking fertility treatment. For reproductive endocrinologists, the tests have value in designing fertility treatment and [selecting the most appropriate fertility treatment protocol](#). They predict response to fertility medications and allow infertility specialists to select treatment protocol and gonadotropin dose. Egg reserve also predicts the number of eggs retrieved for [IVF](#) or [egg freezing](#).

Egg Reserve: Egg Number

Although the number of eggs in the ovaries decrease with age there is significant individual variation in initial number endowed in the ovaries and the rate of decrease. Some young women have low egg number and older women with large number of eggs. Ovarian reserve tests are used to estimate this number.



Egge reserve: the number of eggs in the ovaries drops with age

History

Medical history may indicate low egg reserve in women with prior excision of ovarian cysts, endometriosis of the ovaries, women who smoke and with family history of early menopause

Antral follicle count

The number of antral follicles in the ovaries (the structures that contain the eggs) can be seen and counted using vaginal ultrasound. Performed by an experienced reproductive endocrinologist, it can accurately estimate ovarian reserve. Low count e.g <10 in both ovaries points to low reserve.

Day 3 FSH, Estradiol

FSH is produced by the master gland in the base of the brain. Estradiol is made by the follicles themselves. Measured in the second or third day of menstrual cycle, high FSH (>12) or high

estradiol (>75) points to low egg reserve.

Antimüllerian Hormone (AMH)

AMH is produced by the cells surrounding the eggs in small follicles and is a more direct measure of egg reserve than FSH. It can be accurately measured any day in the cycle with little variations in between cycles. Levels <1.5 ng/dL generally indicates low egg reserve. It correlates well with antral follicle count.

Genetic Screening

Low egg reserve in few women is due to a genetic cause. Fragile X syndrome is a genetic disease that causes low egg reserve and mental deficiency in newborn males. Chromosomal abnormalities e.g Turner syndrome, translocations are also associated with low egg reserve. Genetic screening is performed using a simple blood test before starting fertility treatment.

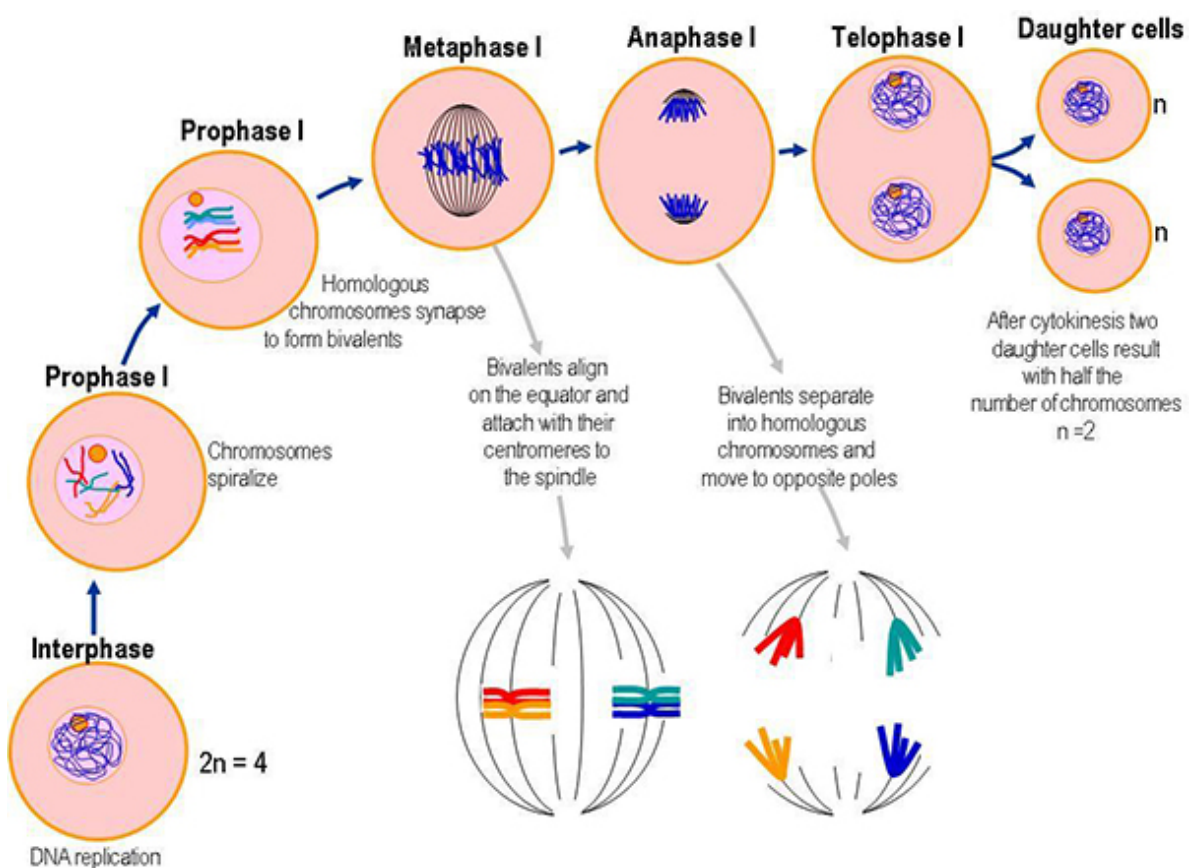
Egg Reserve: Egg Quality

What does egg quality means ?

Good quality eggs are chromosomally normal (has 23 chromosomes). The most important factor that prevents the achievement of pregnancy or leads to early miscarriage is an abnormal egg (has extra or missing chromosome or piece of a chromosome). Many eggs at any age in any woman are abnormal and the normal eggs are the ones that are successful in being fertilized with sperm, implant and achieve a pregnancy. These errors takes place when the original cell that produce the eggs divide to reduce the number of chromosomes to half. The division (meiosis) is many times unequal leading to an egg with an extra or missing chromosome.

Age and egg quality

The ovary releases better quality age earlier in life and lower quality age later, for unknown reason. Female age is the most important indicator for egg quality, chance for spontaneous pregnancy and after fertility treatment. Older women need to try longer to achieve pregnancy and at an increased risk for miscarriage, ectopic pregnancy and delivering a baby with chromosomal abnormalities e.g Down Syndrome. [This effect of age become clinically evident at age 30 or even earlier.](#) Age is more important than the number of eggs in the ovaries. Young women with few eggs in the ovary are more successful in getting pregnant than older women with many eggs in the ovary.



Meiosis

Testing for egg quality: PGD

Age is the only available noninvasive method to estimate egg quality. Healthy eggs cannot be identified using any non invasive method. It is possible to identify chromosomal errors in the egg during IVF fertility treatment after biopsy of the first polar body of unfertilized egg or after removing one cell from an embryo after the egg is fertilized then test this material for chromosomal abnormality. This process is called [PGD or preimplantation genetic diagnosis](#). It is important to remember that PGD is not proven so far as method of enhancing fertility potential. It simply detects if the egg or embryo is chromosomally normal or not but will not make an unhealthy egg healthy.

Read more about ovarian reserve and low response to ovarian stimulation in my review [here](#).