Male Factor Infertility: Azospermia

Male Factor Infertility: Azospermia

Male Factor Infertility: Azospermia means no sperm are found in the ejaculate. Azospermia requires careful evaluation and treatment so that the couple has the best chance to conceive with IVF. The evaluation should be methodical and compassionate to guide the couple through such a multifaceted process to pregnancy and delivery of a healthy child.

Four Things Have to Happen at Initial Evaluation for Azospermia

a. Is it truly azospermia? sometimes repeat sperm analysis together with spinning of the ejaculate multiple times may yield few sperm. This has to be performed by a diligent andrologist and in a facility that can freeze sperm immediately if found. In some azospermic men, repeat analysis and freezing can avoid a surgical procedure to retrieve sperm.

b. A genetic cause for azospermia should be excluded. Specifically three known genetic problems should be excluded because they can be passed to offspring and because they can predict the success of surgical sperm retrieval. A chromosome analysis should be done to exclude sex chromosome abnormalities e.g klinefelter Syndrome (47XXY). Y chromosome microdeletion study should be conducted to exclude a deletion of the part of Y chromosome related to sperm production. Cystic fibrosis carrier screening should also be run to detect defect in the CF gene that may be associated with absence of the ducts conducting the sperm outside of the testes.

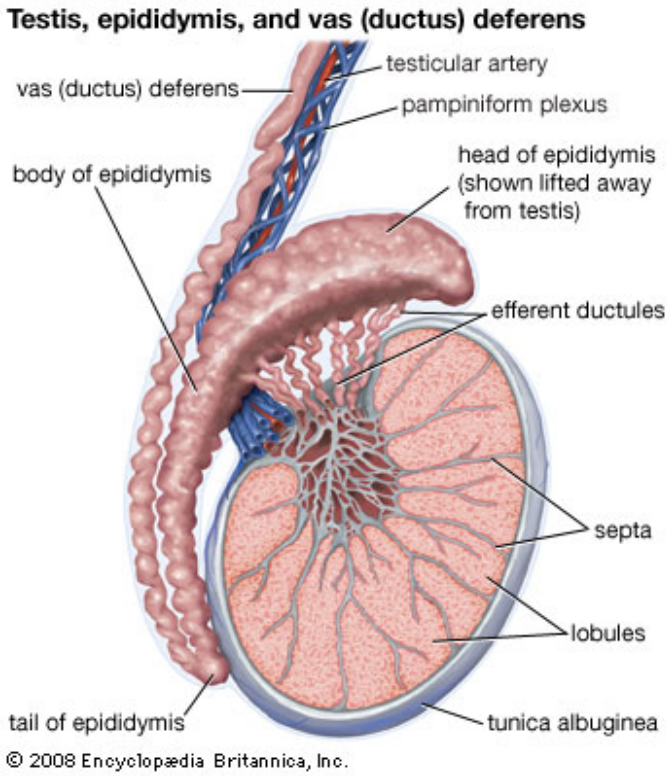
c. Evaluation of Ovarian Reserve for Female Partner. If

ovarian reserve evident by day 3 FSH, AMH levels and antral follicle count seen on vaginal ultrasound is not diminished, this predicts reasonable chance for success with IVF-ICSI if sperm are found. Extremely low ovarian reserve or advanced female age may preclude surgical sperm retrieval, unless an donor eggs are acceptable.

d. Urological evaluation. This has to be the last step in evaluation. Male urologists are the physicians specializing in evaluating the chance for successful sperm retrieval (TESE) as well perform these procedures. Before referral by a reproductive endocrinologist and infertility specialist, there should be every reason to think that if sperm were obtained there is a reasonable chance for conception after IVF-ICSI. The urologist should be a specialist in male reproduction and well versed in the techniques of sperm retrieval. You actually need to ask your urologist two questions: what are my personalized chance for finding sperm when surgery (TESE) is performed? What the technique used to obtain sperm? Authorities generally agree that the technique for TESE markedly affect the chance for finding sperm.

Moreover, every workup should end with an important question; would you accept donor sperm if no sperm were obtained after surgery?

How is TESE Performed?



Testes and ducts

Testicular sperm extraction is a surgical procedure that entails sampling of multiple areas of the testes aiming at finding sperm to be used for IVF-ICSI. The tested is delivered outside the scrotum, bisected and multiple biopsies obtained from several areas of the testes. The tissue is examined for the presence of sperm. If no sperm were found, more biopsies are obtained till sperm are found. There are generally two types of azospermia: obstructive azospermia (due to obstruction of the ducts of the testes while sperm production is intact). Sperm is obtained in close to 100% of these cases. Non-obstructive azospermia (NOA) where is a defect in sperm production, approximately 60 to 70% of the procedures yield sperm.

Blind biopsy from one area of the testes has no place in modern treatment of azospermia. Asking your urologist about the technique of TESE is of paramount importance. The first surgical attempt carries the highest chance for success.

Recently, Doppler ultrasound mapping of the testes can help localize the areas of that should be biopsies because they

yield a higher chance for finding sperm.

Why is IVF-ICSI Required after Sperm Retrieval?

The number of sperm obtained after TESE is small in the magnitude of tens to hundreds of sperm, too small to use the sperm for IUI. ICSI is absolutely required for all cases of surgical retrieval of sperm. The sperm can be used in one of two ways

a. Frozen TESE sperm: The sperm are frozen to be thawed at a later date, on the day of egg retrieval for the female partner. This method saves the cost of IVF if no sperm were retrieved and donor sperm use is unacceptable.

b. Fresh TESE sperm: Ovarian stimulation is started and TESE is performed on the day of egg retrieval or the day before. Fresh sperm are used for ICSI. Donor sperm (if acceptable) is obtained as a backup. Though suggested, there no concrete evidence that fresh TESE sperm is superior to frozen TESE sperm.

In addition in some caes with associated genetic problems, preimplantation genetic diagnosis (PGD) can be performed followed by the transfer of normal embryos.

Can the Chance for Pregnancy be predicted in Male Factor Infertility: Azospermia ?

There are several predictive factors for pregnancy in female partners of men with azospermia. These can be categorized into:

i. Successful sperm retrieval is related to whether the procedure is the first one or a repeat procedure, the volume of the testes, medical treatment before surgery, the technique used and the cause for azospermia. Some causes are associated

to minimal chance for obtaining sperm.

ii. Pregnancy after sperm retrieval is related to the female partner age and her ovarian reserve. Younger women have a very good chance of conceiving if sperm are obtained. This is the most important factor once sperm are retrieved.

iii. Obstructive azospermia has a higher chance for sperm retrieval than non-obstructive azospermia.

iv. Moving sperm at the time of ICSI has a higher chance to yield a pregnancy than non moving sperm

v. Men with higher testosterone levels and lower LH levels has higher chance of sperm retrieval

vi. The effect of using of frozen TESE sperm is controversial. Some authorities think that using a fresh TESE sperm is better than frozen sperm.

vii. Use of Doppler: recent work indicates that the use of Doppler study of the testes before the procedure may help localize the areas that should be biopsies and yield a higher chance for sperm harvest.

> *Male Factor Infertility: Azospermia requires a multidisciplinary approach; first consultation with a reproductive endocrinologist (female age is still the most important factor) followed by a consultation with a reproductive urologist for the TESE procedure for successful sperm harvest and pregnancy*

Endometriosis will not Lower IVF Success

Endometriosis will not Lower IVF Success

Effects of endometriosis on fertility treatment success has always been a controversy. When a woman is diagnosed with endometriosis, she receives multiple contradicting advises from multiple sources. It is very difficult for women to sort through these recommendations and pick the ***one that are suitable for her symptoms and reproductive plans***. Indeed reproductive plans and symptoms are by far more important than the nature of the problem, anatomically, as well as what one reproductive surgeon or a fertility specialist think you should do.

Reproductive Plans in women diagnosed with endometriosis

Simply do you want to fave a baby or did you complete your family?. If you want to have a baby, then an initial infertility evaluation is required: testing for ovulation, ovarian reserve, male factor and Fallopian tube patency is required. Sometimes other forms of pelvic imaging e.g MRI is needed to test for ovarian cysts or endometriomas…Endometriosis itself may require laparoscopy and biopsy for accurate diagnosis.

Women are then categorized according to findings: endometriosis only, endometriosis with other factor or endometriosis with low egg reserve. That will facilitate further advice.

One very important indicator that you are not talking to the right person if he or she did not complete the evaluation for male factor and egg reserve. These are essential tenets of fertility and failure to test them will have impact on success. It would be absurd to do surgery for endometriosis for example to discover later that you have a severe male factor that require IVF -ICSI.

If you desire future fertility, reproductive endocrinologists should taylor their advice to preserve reproductive tissues and minimize surgery. There is a strong evidence that surgery in the ovary reduces ovarian reserve, irrespective of technique used.

Pain in women diagnosed with endometriosis

If the main symptom is pain, in different forms, then medical or surgical treatment can be employed. in women who completed their families. Medical treatment e.g non cyclic oral contraceptive pills of GnRH agonists (depot lupron) prevent pregnancy. From a practical stand point, surgery im many cases may not promote pregnancy in women with with mild and severe endometriosis.

> ***Women diagnosed with endometriosis and report pelvic pain should focus on getting pregnant. Pregnancy can suppress endometriosis for a long time after delivery***

Fertility Treatment in Women Diagnosed with Endometriosis

Absolutely avoid doing surgery in the ovaries in women interested in pregnancy. This is crucial. Opening endometriomas and tripping their walls leads to significant loss of egg reserve. The only indication to remove endometriomas if they are complicated e.g rupture or suspicion

of malignancy. There are many reports of finding eggs in the wall of endometriomas after removal and reduction in egg reserve markers after surgery. Bilateral surgery for endometioma can lead to menopause, irrespective of the skill of the surgeon.

In minimal and mild endometriosis with reasonable egg reserve, normal sperm analysis and open fallopian tubes, ovarian stimulation and IUI can be entertained in young women (38 years).

In women with moderate or severe endometriosis e.g endometriomas, blocked tubes.. or those with associated male factor infertility or low egg reserve, IVF yields a much higher pregnancy rate.

IVF Success in Women with Endometriosis

Recent analysis of IVF cycles performed in women with endometriosis with or without other factors (tubal, male, unexplained infertility) indicates that

Isolated endometriosis is associated with similar IVF success and live birth to other infertility factors, though the number of eggs retrieved may be smaller.

Endometriosis when associated with other factors e.g male or tubal factor may have lower success rates. The live birth rate is still excellent 35 to 45% per cycle.

Endometriosis-and-IVF

Treatment of Endometriosis related pain

Both medical treatment and surgery are effective for treatment of pain. Endometriomas do not respond to medical treatment. Endometriosis on the peitoneum and and other organs respond to medical and surgical treatment. Adenomyosis (endometriosis of

the uterus) is a surgical disease and respond only to surgery.

In general medical treatment is successful but requires patience and can be used for a longer period of time with add back therapy.

If you are diagnosed with endometriosis there is wide range of treatment options. Treatment should be personalized to your reproductive goals and symptoms not to physician expertise and bias. There is really little controversy about what need to be done in each situation. Women just need to be specific about what they want: get rid of pain or have another baby. IVF success is not impaired in women with endometriosis.

Medically + Economically You Should Avoid IUI at Age 38

Medically + Economically You Should Avoid IUI at Age 38

Medically and Economically you should void IUI at age 38 or older. Couples facing difficulty conceiving and after completing a fertility workup, they have three general fertility treatment options. Regular intercourse, ovarian stimulation with oral medications (clomid or letrozole) or injection medications followed by IUI (COH-IUI) or IVF.

The chance for pregnancy is very low with COH-IUI that you may as well just try with intercourse. The likely cause is production of a small number of eggs with these stimulation protocols, lowering the chance of encountering a chromosomally normal eggs. IUI in itself slightly increases the pregnancy

rate but the main benefit in fertility treatment is produced through ovarian stimulation and recruitment of multiple eggs.

On the other hand, IVF carries a very good chance for getting pregnant. If not ready for fertility treatment just have regular intercourse. If ready, proceed directly to IVF as you will realize much higher success rate and save also on treatment with minimal yield (IUI). Here is a synopsis of published studies (asrm.org).

Traditional egg reserve tests

Women who initiated infertility treatment with FSH of 10 to 15 mIU/mL and E >40 pg/mL on day 3 testing were unlikely to achieve live birth after COH-IUI treatment. In two well designed studies on 603 patients contributing 2,717 total cycles, no live births occurred during COH-IUI. IVF still afforded these patients a reasonable chance of success (6/18 couples, 6/40 cycles, 33.3% live-birth rate per couple).

Female Age

Age ≥ 38 to 42y:

The *cumulative clinical pregnancy rates per couple after the first two cycles of CC/IUI, FSH/IUI, or immediate IVF were 21.6%, 17.3%, and 49.0%*, respectively. After all treatments, 110 (71.4%) of 154 couples had conceived a clinically recognized pregnancy, and 46.1% had delivered at least one live-born baby; 84.2% of all live-born infants resulting from treatment were achieved via IVF. There were 36% fewer treatment cycles in the IVF arm compared with either COH/IUI arm. Also couples conceived a pregnancy leading to a live birth after fewer treatment cycles.

Age 21-39:
Per cycle pregnancy rates for CC/IUI, FSH/IUI, and IVF were **7.6%, 9.8%, and 30.7%**, respectively. Average charges per delivery were $9,800 lower ($25,100 lower to $3,900 higher) in

the accelerated arm (IVF) compared to conventional treatment (IUI).

Other Fertility and Social Factors to consider

There are other factors to consider: moderate to severe male factor and blocked tubes makes IUI and intercourse not an option. Absolute cost and insurance coverage are maybe important (although its by far more cost effective). Risk of multiple pregnancy should always be considered especially with Injection +IUI cycles. Some couples have personal ” resistance” to adopting IVF as difficult, uncomfortable, risky or unnatural, and that autonomy has to be both respected and embraced but also discussed. Their sentiment has to be balanced against a 7% per cycle pregnancy rate if you do Clomid-IUI, 9% per cycle injection -IUI (both become zero if egg reserve tests are abnormal) *versus* 35%pregnancy rate with IVF.
Knowing the expected rate of success is an integral part of fertility counseling.

Medically + Economically you should avoid IUI at age 38

> *All being equal, for modern couples, the most humane approach is to get them pregnant before the short favorable window of reasonable number and quality of eggs wane. No to do so means letting them enter the into the more difficult phase of final reproductive years. Treatment ssuccess drops in late reproductive years to a single digit and they jeopardize their chance of having a baby.*

FORTT

Melanoma-What Every Woman Need to Know about Fertility and Pregnancy

Women diagnosed with melanoma may require counseling for fertility preservation, fertility treatment and safety of pregnancy after treatment. Melanoma is one of the most common cancers in young adults in the United States. In the US and worldwide, there is dramatic increase in the incidence of skin melanomas. Approximately 30,000 women are expected to be diagnosed with melanoma in 2010, one third will be in their reproductive years. Its the most common cancer in young adults 25 to 29 year old. Its more common in white women compared to African Americans and Hispanics. Approximately 10% of melanomas run in families or are genetically inherited. Treatment of melanoma requires surgery. In advanced melanoma, chemotherapy is added. Dacarbazine-DTIC is an alkylating agent used for treating melanomas. Immune therapy is also used for advanced melanomas-interferon α or IL-2.

In early stages, surgery is the only required treatment. In advanced stages if chemotherapy is used, ovarian reserve may be diminished and this may reduce woman's ability to get pregnant. The use of immune therapy is not known to affect future fertility. The effects of newer targeted therapies and vaccines on fertility are also unknown.

Melanoma and fertility treatment. The estrogen receptors were

found on melanoma cells. Some researchers detected no significant increase in the risk of melanoma after treatment with fertility drugs, except possibly slight increase in risk in women who delivered children before. The relationship between estrogen exposure and melanoma is controversial. Women seeking fertility preservation before exposure to chemotherapy or melanoma survivors desiring pregnancy after completing treatment should consult with a fertility preservation specialist about the risks and benefits of fertility treatment and the safety of pregnancy. The ovarian stimulation regimen can also be modified to minimize estrogen exposure. It may also be possible for women with inherited predisposition to melanoma to avoid transmission to future children through testing of embryos-PGD.

Melanoma and pregnancy. Ten studies including 5600 women found that pregnancy does not reduce survival in women diagnosed with melanoma. Women treated for melanoma who subsequently became pregnant were not adversely affected compared to women who did not get pregnant after treatment. For thin tumors-<1.5mm most experts do not recommend deferring pregnancy. For thicker tumors, physicians may recommend deferring pregnancy for two years as most recurrences take place during that interval. Read more at http://nycivf.org

What if You Have Dual Infertility Factor

What if You Have Dual Infertility Factor

Many Times You Do

Infertility factors are generally classified into tubal factor (blocked fallopian tubes), male factor (abnormal sperm concentration, movement or shape) and ovarian factor (no ovulation). In the majority of situations though multiple factors exist. If you partner has low sperm count, you also may have a blocked tube. Women who do not ovulate can also have endometriosis. Some men think that their female partners are infertile due to a female factor while they also have subtle sperm abnormality that prevents fertilization. Women sometimes think their male partners sperm is abnormal while they also have low egg reserve and low egg quality. *Couples potentially have a dual infertility factor, most of the time*. Most notably, low egg number and quality should be considered in any couple seeking fertility evaluation and treatment. Even young women with good egg reserve have abnormal eggs.

Irrespective of infertility factors, consideration of other general factors e.g genetic screening results can have a significant impact on choice of fertility treatment modality. If both partners are carriers for cystic fibrosis, they may require embryo testing (PGD) in the setting of IVF as opposed tosimilar couples without this genetic risk factor.

Do not Accept Treatment Before a Complete Workup. Do not Accept Empiric Treatments

For that reason, no assumptions about fertility factors and treatment should be made before a completed workup for sperm, ovulation, ovarian reserve, Fallopian tubes and general

factors (genetic and preconception screening). This careful and deliberate testing is unfortunately not always followed. In many cases, couples are treated with empiric treatments. Here are two very common empiric treatments commonly prescribed

a. Clomid used for everyone. Clomiphene is suitable as initial treatment for women who do not ovulate due to polycystic ovary syndrome (PCOS), have open tubes and normal sperm analysis. In modern reproductive medicine, clomid should not be used without testing of male and tubal factor. Clomid also should not be used in older women that ovulate regularly. The majority of these women are older and do not get pregnant because of lower egg quality. They require superovulation (more than one eggs) to compensate for lower egg quality.

b. Progesterone supplementation. Low progesterone can cause early miscarriage (not infertility) in a small percentage of women. Women that yield low progesterone after ovulation do so because of abnormal development of follicles. They are better served by induction of ovulation to produce better follicles, rather than progesterone supplementation. During fertility treatment, progesterone levels are monitored and maybe supplemented if low. Progesterone treatment in itself is not a treatment for any form of infertility.

c. Laparoscopic surgery for endometriosis. The magnitude of benefit for surgical treatment of infertility associated with endometriosis is limited and maybe harmful. Laparoscopic surgery for severe endometriosis is risky e.g bowel injury. Resection of endometrioma can reduce ovarian reserve. IVF is a better than laparoscopic surgery in treating infertility due to moderate and severe endometriosis . The increase in pregnancy rate after excision of mild endometriosis is limited (probably 30 surgeries are needed to produce one newborn).

d. Varicocele repair for male factor infertility. Although sperm parameters may improve after varicocele repair, there is

no conclusive evidence that it will translate into higher odds of pregnancy in female partners. There is a limited indication for varicocele repair aiming at improving fertility in males.

Many of these empiric treatments and prescribed with no or limited scientific basis and represent bias and expertise of the prescriber.

How to Select an Egg Donor

How to Select an Egg Donor

Egg donation entails the fertilization of eggs of a young woman and transfer of the resulting embryo or embryos into the intended mother uterus. In the majority of cases, women are interested in egg donation when their ovarian reserve is diminished in quantity and quality, commonly after multiple unsuccessful IVF cycles. The eggs of young women are usually high in quality making the chance for pregnancy and delivery very high. Women can select an egg donor from one of two pools

Egg Donors

Eggs from a Live Donor

An young woman is selected for donation, her ovaries are stimulated then eggs are retrieved. Two types of egg donors exist:

i. Known Egg donor

The egg donor is known to the intended mother. The donor could be a related e.g. sister or not a relative but agreed to open identity egg donation.

ii. Anonymous Egg donor

The egg donor is not known to the recipient. The majority of eggs donated are contributed by anonymous donors. If you select a closed identity donor you will still be able to know a great deal about her as age, ethnicity, religion, education, medical and family history, prior donations, physical features, childhood or even adult photo. Anonymous egg donors are usually recruited by a third party: IVF clinic or an egg donation agency. Shared Donor cycle: Sometimes the eggs from one donor are shared between two recipients to reduce cost. Sharing however may yield lower chance for pregnancy per couple.

Donor Egg Bank

An egg bank will recruit the donors, stimulate their ovaries and freeze them. Recipient select from an already frozen inventory. The advantage is that they do not need to wait for a donor to be found, tested and her eggs harvested. In addition it is cheaper because only some of the eggs resulting from stimulation are obtained and no expenses incurred for donor travel and accommodation. On the other hand, it may yield lower chance for pregnancy (eggs are frozen and fewer of them are available). Donor selection is also restricted to available inventory of eggs that were already donated at an earlier time.

Results of Donor Egg Cycles Based on Donor Selection

Based on hundreds of thousands of donor egg cycles some general expectations of pregnancy and live birth rates can be made:

a. Anonymous cycles usually yields a higher pregnancy rates than known donors. Anonymous donors are selected on pure medical grounds first. They tend to have better ovarian reserve and are commonly younger than known donors. Many times known donors are based on other grounds e.g sister donor or a friend that will donate without compensation

b. Donor egg cycles distributed to one recipient are more successful than those shared between two recipients due to more eggs and embryos being available for selection and transfer.

c. Fresh eggs from live donors produce more babies than frozen donor eggs. A study of 11,148 egg donation cycles performed in 380 U.S. clinics in 2013, including 2,227 that used frozen eggs indicated that

for each IVF cycle the live birth rates were 50% with fresh eggs, and 43% with frozen eggs and

for each embryo transfer, 56% of embryos created with fresh eggs resulted in a live birth, compared to 47% of embryos created with frozen eggs.

The Process of Selecting an Egg Donor

The process of selecting an egg donor is complex that involves you, your partner, your reproductive endocrinologist and sometimes other parties. The guiding principals for selecting a donor are

a. Selecting a donor with good ovarian reserve b. Protecting the mother from the transmission of infectious

diseases c. Protecting the babies from the transmission of genetic diseases d. Protection of the egg donor from potential complications of IVF e. Partners preferences.

Ovarian reserve: an egg donor should have an excellent ovarian reserve. This predicts excellent response to treatment with fertility medications and the collection of large number of mature goo quality eggs. Egg reserve is assessed through history taking, vaginal ultrasound estimation of antral follicle count, day 3 FSH and estradiol assay and AMH levels. Donors should be younger than 32 years and preferably younger than 30.

Infectious disease screening: donor are screened using first a thorough history and examination. Donor practicing in high risk behavior and those that lived in certain geographical areas are excluded. Lab tests are obtained for hepatitis B, hepatitis C, HIV I/II, Syphilis, gonorrhea and chlamydia. Other tests for infectious diseases could include testing for human T lymphocyte virus I/II, West Nile virus and South American trypanosomiasis. Tests are run at initial encounter then repeated in specialized labs within 30 days of retrieval to minimize the possibility of acquiring any of these infections at a later time.

Genetic screening: Extensive genetic and family history is first obtained from the donor. This is followed by screening for at minimal cystic fibrosis and any genetic disease related to donor ethnicity e.g hemoglobin abnormalities in African, Asian and Meditranean donors-Ashkenazi pannel in Jewish donors. Spinal muscular atrophy and fragile X syndromes are commonly also screened. More recently a universal genetic test that include 100 most common genetic diseases is routinely used. If an abnormality is found, a genetic counselor is consulted.

Donor related precautions: Egg donors should have the ability and intelligence to understand the process. This is evaluated

by a trained psychologist. egg donors are counseled that the process does not impair their ability to conceive children of her own. Stimulation is tailored to avoid excessive stimulation and ovarian hyperstimulation syndrome. Donor are followed up after the procedure to monitor for any complications form retrieval and that the ovaries regained their normal size after stimulation.

Partners preference: Partners are offered a session with a psychologist to express their feelings about the process and to discuss some of the early and long term aspects of the process inducing legal issues an disclosure to children when they reach maturity. Partners may prefer certain race or ethnicity e.g Asian, Jewish…Some agencies specialize in recruiting donors of specific demographics. Physical features are also strongly considered and discussed with couples. Academic achievements are also desired by many couples.

Other considerations: Male partner sperm analysis and labs are obtained. The mother is assessed for any medical disorder and the ability to carry a pregnancy safely. The uterine cavity is evaluated using hysteroscopy or saline sonography. The endometrium is evaluated for its response to hormones. The cervix is mapped to avoid difficult embryo transfer.

The process of egg donation is commonly satisfying to recipients, donors and physicians and is flexible to allow for safe selection of an egg donor and still consider your preferences and aspirations.

Testosterone Therapy-Male

Infertility

Testosterone Therapy-Male Infertility

Many men are prescribed testosterone for a variety of reasons. Low testosterone levels (Low T) with no symptoms, general symptoms of low energy and feeling tiered and sexual symptoms, among others. Approximately 2.5 million men are prescribed testosterone each year in The US, mostly with no proper testing. Testosterone is only approved by FDA for low testosterone associated with specific diseases affecting testicular function. The FDA recently issued a safety communication cautioning the use of testosterone replacement for low testosterone levels and requiring labeling change to inform men of a possible increase in side effects.

From the fertility standpoint, there is no role for testosterone treatment, that could be detrimental. There is also no *proven* role for other medical treatment as clomid, letrozole, nolvadex, hCG and others in enhancing fertility in the vast majority of men

Effects of testosterone on male fertility

When men are prescribed testosterone, sperm production slows down significantly and may completely stop. Many of them, no sperm can be found in the ejaculate (azospermia). Testosterone therapy can markedly lower the ability of men to father children. Testosterone inhibits a key master gland hormone (FSH) that is required to stimulate spermatogenesis (making sperm). The specific effects of testosterone on sperm count are unpredictable. In some men sperm count drops to zero even after a short use of testosterone.

Interestingly, when testosterone is stopped some men but definitely not all of them recover sperm production, commonly in one to six months. The extent of the recovery of sperm

count is also unpredictable. The recovery of sperm count maybe limited requiring fertility treatment for conception to take place. A short course of testosterone can lead to a low sperm count for a very long time.

What can be done about low sperm count related to testosterone treatment

In addition to evaluation of female factors especially ovarian reserve, always a priority, men on testosterone and showing low sperm count should be advised to

1. Stop testosterone administration immediately

2. Repeat sperm analysis in 2 months. Sperm analysis should be performed in a facility that can perform diligent search for even very few sperm and can freeze sperm. If sperm is found in the ejaculate it should be cryopreserved immediately. If no sperm is found then sperm analysis should be repeated in another 2 months. The wait for recovery cannot be indefinite because of further deterioration of ovarian reserve in female partner with time.

3. Depending on the extent of recovery sperm can be utilized to promote conception. If sperm count recover close to 10 million moving sperm, natural conception can take place. Also sperm can be used for IUI, if needed. If the number of motile sperm is significantly lower, IVF is required, sometimes with intracytoplasmic sperm injection (ICSI).

4. If still no sperm were found after repeat analysis, TESE (testicular sperm extraction) can be attempted. A male reproductive urologist can perform diligent search for areas of spermatogenesis in the testes through repeat minute biopsy and searching under the microscope.

From the preventive aspect, avoid testosterone treatment if you intend to father children in the future. Know that there are very few solid indications for testosterone. If

testosterone treatment is inevitable, consider pretreatment sperm freezing. Use gel preparation preferential to injection as they are not stored for a long time in the body.

Testosterone treatment is a preventable cause for infertility in males and could be detrimental to future fertility.

Why are You Afraid of Infertility Treatment (and generally should not)

Why are You Afraid of Infertility Treatment (and generally should not)

When have been trying to conceive for a while, women and men often are reluctant to seek help from a fertility specialist. What if they told me you cannot conceive? what if they find a major problem with my fertility? what if I need extensive treatment? All are viable questions. One deviation at that point is to consult with a specialist in your immediate circle but in another discipline: gynecologist or internist. This deprives you from valuable resources and tend to underestimate any issues you may have. This is a very common reaction in general use of supplements instead of medicine, go to a holistic specialist instead of a physician..

Why are you afraid of Fertility Consultation

When you consult with a reproductive endocrinologist you may anxious about a discovery of one or more fertility issues, that may require treatment. Fertility problems are very

private, maybe more than any other medical problems. They are certainly more private, though less risky, than heart disease or intestinal problems. You are also worried about the treatment of such factors and the required time and financial resources. One evidence of evidence of such fear is reluctance to seek consultation for years sometimes.

Why are you afraid of fertility treatment

Once you start a consultation with a fertility specialist and treatment is recommended, couples are worried about the treatment process: complications and results.

Possible Complications of Fertility Treatment

All the complications of fertility can be classified into proven complications and unproven complications

Proven Complications

i. Multiple Pregnancy

Multiple pregnancy

Twins and higher order multiple pregnancy is an established complication of fertility treatment. It is directly related to the type of treatment (IUI or IVF), age and the number of embryos (IVF) transferred or follicles observed (IUI). The

general incidence of twins is 1% after natural conception, 30% after IUI or two or more embryo transfer and 1% after single embryo transfer. The general incidence of triplets or higher is less than 0.1% after natural conception and 3% following fertility treatment.

ii. Ovarian Hyperstimulation Syndrome

Also an established complication of ovarian stimulation. It is more common in younger patients with large number of antral follicles seen in the ovary and high AMH levels. Women with PCOS are particularly at risk. The incidence of sever forms is 0.5 to 1%. In its severe forms it may lead to accumulation of fluid in the abdomen, blood clotting and may require hospital admission.

iii. Complications from egg retrieval

Egg retrieval is associated with very low level of comlications <1/1000, including bleeding, infection and anesthetic complication.

iv. Pregnancy Complications

Like any pregnancy there is a risk for miscarriage (15%) and ectopic pregnancy (3%) (e.g pregnancy in the fallopian tubes).

Unproven Complications

Cancer

There is no conclusive evidence that ovarian stimulation or any fertility treatment, in itself, increases the risk of cancer (any type). It is true that women who delay conceiving are at an increased risk for some types of cancer e.g breast cancer, ovarian cancer…There is however no proof that there is an increased risk of cancer *due to treatment*. For example, the risk for breast cancer in women living in the US is 1 in 8. This risk is slightly increased for women who deliver their first child after age 30. If a woman decided to undergo

fertility treatment, her risk for breast cancer is not increased say to 1 in 6 because of that above her baseline risk

Congenital abnormalities

There is also no conclusive evidence that congenital abnormalities in babies conceived after fertility treatment is significantly increased after fertility treatment, for the vast majority of couples. In any population in the world, the incidence of birth defects after natural conception is 3-4% (not zero). This is the baseline risk. If a couple undergo fertility treatment, there no proof that that incidence is increased, say to 5%, compared to couples that declined fertility treatment. Many women seeking fertility treatment are older and are at increased risk for chromosomal abnormalities. Also infertility itself appear to be a risk for factor for slight increase in birth defects. But there is no evidence that medical procedures themselves increases the risk for congenital abnormalities. There are some special situations e.g severe male factor that even associated with further increase in risk of abnormalites, so a couple specific risk should be discussed with your reproductive endocrinologist. Note also that becoming pregnant at a younger age (with or without fertility treatment) reduces your risk for chromosomal abnormalities.

Results

You are certainly worried about the result of fertility treatment. That may make some women fearful of proceeding with treatment. Do confront this heads on. Ask your reproductive endocrinologist to give you a customized chance for pregnancy and delivery. Generally, fertility treatment is ultimately very successful. Over 60% of women seeking treatment ultimately deliver a baby or more after fertility intervention. There are many factors that indicate high chance for success, prior to starting treatment: age, ovarian reserve

markers, the order of the cycle (first and second cycles are more successful)..

Long Term Effects

Outcomes of babies and young adults conceived after ovarian stimulation and IVF are definitely a long term concern. The first baby conceived at delivered following IVF was in 1978. Since then, approximately 1% of the world population are born after IVF. The scientific community have long term follow up data on babies born after fresh and frozen embryo transfer. There is even data on the third generation of babies (children of women who were conceived after IVF).

Egg freezing recently gained ground into as a procedure that broadens reproductive options for women. There are no long term data, nor a large number of babies (millions) conceived after egg thawing.

Why you should not be afraid of fertility consultation and fertility treatment

Fertility Consultation

The majority of women undergoing a fertility consultation turns out to have no specific fertility factors and simply regular intercourse is advised. A fertility consultation is crucial in identifying risk factors (e.g genetic, multiple pregnancy) and to estimate odds for a healthy baby without or with treatment. Here is an example. A Caucasian couple are seeking fertility treatment. No fertility factors found, female partner is young. The only abnormality found is that they are both carrier for cystic fibrosis gene mutation (risk of transmission to baby is 25%). Same example apply to an African American couple in the case of sickle cell anemia. Would you want to know this? Another example, you are young but on fertility testing it was found that both of your fallopian tubes are blocked and you may need help conceiving. Is this an important information for you to know? Knowledge is

very important, even if you decide not act upon.

Fertility Treatment Complications

Multiple pregnancy: is definitely the most dreaded complication of fertility treatment. There are many steps in evaluation and treatment that can minimize the risk of multiple pregnancy to a rate close to natural conception. Avoiding ovarian stimulation and IUI in favour of IVF with single embryo transfer appears to be the most important treatment decision that can minimize multiple pregnancy. IUI appears more conservative but actually that is not true. IVF with a single embryo transfer is more conservative due to lower risk for multiple pregnancy. Acceptability of fetal reduction is also another issue that should be discussed before starting treatment. The indiscriminate use of clomid appears to contribute the largest magnitude of risk for multiple pregnancy due to its widespread use without monitoring.

Ovarian Hyperstimulation Syndrome: is largely preventable complication through judicious use of fertility medication and avoiding the use of hCG as a trigger shot in favor of using lupron. An astute reproductive endocrinologist is able to keep this complication to a bear minimum.

Fertility Treatment Results

From one aspect the success rate of fertility treatment (per treatment cycle) is a factor of female medical factors and quality of fertility treatment she receives, if needed. On the other hand, the majority of courageous women who persevere, do get pregnant with fertility treatment. Those who are very unlikely to conceive are identified early on during evaluation and are should counseled accordingly. Women who do get pregnant do not write about it in lay media. Because the chance for conception is personal, you should seek to know your own chance for conceiving fertility treatment success,

paying no attention to what your peers say or what you read. They cannot in any way reflect your own odds for success.

Long term effects of fertility treatment

Data on long term outcomes of young adult conceived with fertility treatment are reassuring of normal development and no significant abnormalities. In relation to egg freezing, there are reports of about a 1000 babies followed for short interval. They appear to show no increase in abnormalities. There are no long term follow up studies of babies conceived from thawed eggs.

The anxiousness about fertility treatment is natural, considering its intimate relationship to our life. Input from lay media and peer anecdotal stories is skewed and not readily applicable to anyone else. Irrespective of the decisions you make, knowing the facts about fertility treatment, personalized to your own personal medical reality is probably empowering and can prevent harm even if you decide not to pursue fertility treatment.

Endometriosis: Fertility Options are Clear

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Endometriosis means tissue of the lining of the uterus is present outside the its normal boundaries. It can involve the pelvic lining, the ovaries (endometrioma), the fallopian tubes, the intestine and the muscle of the uterus

(adenomyosis). As menstruation takes place in the uterus, these deposits menstruate into itself, become distended and causes pain (pain with menstruation, chronic pelvic pain, pain with intercourse, urination or defecation). Moreover, because of its chemical effects or associated pelvic scarring endometriosis may cause infertility.

Accurate diagnosis of endometriosis requires laparoscopy and biopsy of the areas suspicious because of its appearance. If you are suspect you have endometriosis (usually because of pelvic pain) and want to get pregnant or having difficulty becoming pregnant you face a small dilemma. You are usually given different recommendations from different headquarters, depending on their expertise and biases. Examples of such recommendations:

‘Lets do laparoscopy to diagnose endometriosis, remove any endometriosis we find as well as remove any scarring’

‘Lets give you medications for endometriosis’

The questions is which recommendation is “good for your specific case”.

Few basic principals about endometriosis treatment

These are not disputed principals, just facts related to the treatment of endometriosis in general.

1. Accurate diagnosis of endometriosis requires a laparoscopy and pathological examination of tissue biopsies obtained.

2. Medical treatment of endometriosis does not allow you to get pregnant while you are using it: oral contraceptive pills, synthetic progesteron, danazol and GnRH agonists (lupron) prevent ovulation. While you are taking these medications you will mostly not ovulate so you will not get pregnant.

3. Endometriomas (endometriotic cysts of the ovary) do not respond to medical treatment. Moreover their removal mostly

require removal of a part of the ovary, because they are firmly attached. Thus their removal can lower the number of eggs remaining in the ovaries (ovarian reserve).

Treatment of infertility associated with endometriosis

Though each specific situation may require a different course of action as recommended by your physician, there are general guiding principals for treatment of infertility when endometriosis is suspected.

1. Infertility investigation: do not make any treatment decisions without a full fertility workup. Do not proceed unless you know your partner sperm analysis, obtained the results of ovarian reserve tests, tested if your fallopian tubes are open or not via an HSG as well as general preconception lab tests. Why? if you undergo surgical treatment for endometriosis and later discovered that your partner has very low sperm count requiring IVF and ICSI, then surgery had no potential to help you get pregnant.

2. What is your priority treating infertility or treating pain? This is important because medical treatment, although effective in treating pain cannot help you with infertility because it mostly prevents ovulation. Please note that the best treatment for pain associated with infertility is pregnancy. The large amounts of progesterone produced during pregnancy suppresses endometriosis, sometimes for years after delivery.

3. Resection of endometrioma; If a cyst consistent with endometriosis is seen on ultrasound be very careful with a recommendation to resect that cyst. Resection requires surgery. it reduces ovarian reserve because of removal of ovarian tissue. Unless the cyst is suspicious of malignancy or complication they are better left alone with observation while proceeding directly to fertility treatment e.g IVF. There is

no evidence that removal of the cyst improves IVF success. On the contrary, removal of the cyst is associated with low response in that ovary.

4. Laparoscopis surgery for mild and minimal endometriosis: There are two studies that showed an improvement in pregnancy rate after laparoscopy for mild endometriosis. To put this in perspective, yes laparoscopy for infertility and mild endometriosis and infertility is an option but the magnitude of benefit in this case is limited at best. You first have to undergo surgery (with its possible complications). If endometriosis is found and ablated you would get a small bump in pregnancy rate in the year following surgery. The surgery may also help you with pain. On the contrary, endometriosis may not be found and you still have to try after surgery. Considering all the risks and benefits, the odds for pregnancy is not dramatically improved.

5. An alternative approach to mild and minimal endometriosis: The general thinking about infertility associated with minimal and mild endometriosis is that it is unexplained infertility. In these cases there is no mechanical distortion of pelvic organs and fallopian tubes are open. If sperm analysis is within normal enhancing fertility could be achieved through stimulation of the ovary to produce multiple eggs followed by IUI or IVF. This approach avoids surgery with its potential complication. IVF carries approximately three times the odds of pregnancy and can control the risk for multiple pregnancy, compared to IUI.

6. Moderate to severe endometriosis: These cause distortion or blocking of the fallopian tubes. Surgery is an option but its much more complicated than mild cases and has the risk of injury to the intestine, ureter, fallopian tubes, oavries..Scarring also may recur after surgery. An alternative approach is to proceed to IVF. It avoids major surgery and can address tubal, male and ovulatory factors. IVF success is not reduced in women with endometriosis.

7. Adenomysis (endometriosis of the uterus): MRI is sometimes needed for accurate diagnosis of adenomyosis. Adenomyosis is a surgical disease and its cure require removal of the whole uterus. This is because it cannot be shelled out of the uterus like a fibroid. Better ignored and proceed with fertility treatment.

Do not make any decisions related to infertility before a complete workup; sperm analysis, ovarian reserve tests and fallopian tube patency test. Avoid surgery in the ovary as it may reduce ovarian reserve. There is no established evidence that the chance for successful fertility treatment is reduced in women with endometriosis. Laparoscopic surgery is an option but is associated with surgical complications.

Egg Freezing what Do you Hope to Accomplish?

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The best approach motherhood is to actually try to get pregnant. Though methods of fertility preservation are very helpful, none is a guarantee to make a baby in the future. So the primary advice is “try to get pregnant if you can” after checking different fertility factors (male, tubal and ovarian factors as well preconception screening). If getting pregnant is not feasible in the short term, due to medical or social issues, egg freezing is considered. *A reproductive endocrinologist is faced with the challenge of foreseeing if a*

specific woman, when stimulated and her eggs are harvested and frozen, has a reasonable potential to conceive using these eggs at one time in the future.

Indication for Egg Freezing

Women should consider egg freezing when specific medical or age related situations threatens their ability to have a child in the future.

1. Fertility preservation: When a medical disorder or its treatment can diminish ovarian reserve and reduce the chance for conception e.g cancer treatment (most common is breast cancer), lupus nephritis requiring treatment with chemotherapy, blood diseases requiring bone marrow transplantation, premature ovarian dysfunction and others. About 2 weeks should be available for an egg freezing cycle.

2. Fertility extension (no male partner): women with no male partner and declining the use of donor sperm can freeze their eggs to use in the future when in a committed relationship.

3. Fertility extension (with a male partner): women with a male partner can elect to freeze some of their eggs unfertilized. Unfertilized eggs are under the control of the woman alone, unlike embryos that cannot be used without the consent of both partners.

4. IVF with failed sperm retrieval or ejaculation: In some cases with male factor with failed retrieval of sperm from the testes or failed ejaculation, eggs can be frozen and used later when sperm are available.

5. Children undergoing treatment for cancer and other diseases with the ascent of their parents.

What should you consider before proceeding to egg freezing

i. Women <38 years with good ovarian reserve: are excellent

candidates for egg freezing. Good reserve is indicated by antral follicle count >10 as seen on vaginal ultrasound and AMH levels > 1.75 ng/mL. They will likely produce a good number of oocytes to freeze in a single cycle. These eggs are relatively healthy as they are young. Age <36 years was the best predictor of egg freezing so far in scientific reports.

ii. Women <38 years with diminished ovarian reserve: are still good candidates for egg freezing. They produce lower number of eggs after stimulation but their oocytes are relatively healthy (chromosomally normal). They can undergo more than one cycle of egg freezing if the first cycle yields <8 mature eggs.

iii. Women 38-40 years with good reserve: can still consider egg freezing with no further delay.

vi. Women 38-40 years with diminished ovarian reserve: should consider egg freezing with caution. They will not produce a good number of eggs and may require multiple cycles of egg freezing.

V. Women >41y are not good candidates for egg freezing even if they have a good reserve as the majority of their oocytes are not chromosomally normal. Although pregnancies were reported from vitrified oocytes up to age 44, the chance of pregnancy in quite low in women older than 40.

Realistic Expectations for egg freezing

Not only should the number and quality of eggs be considered, but also the survival of thawed eggs, fertilization and ultimate ability to implant. These issues are very sensitive to the method of ovarian freezing. Vitrification (rapid freezing) is not the method of choice for low temperature storage of eggs due to high survival and subsequently fertilization and embryo development (more details here and here).

Survival on average 85% of virified thawed eggs survive, irrespective of age.

Fertilization approximately 80% of thawed eggs fertilize after injecting each with a sperm (ICSI).

Age specific chance for a live birth after thawing of vitrified eggs can be presented in different ways. The delivery rate is approximately 5 to 15% per thawed egg depending upon the female age at freezing. For example, if eggs are thawed and fertilized and three embryos were transferred to the uterus, the probability of delivery would be 25% at age 30 and 15% at age 40.

If a 35 year old decided to proceed with an egg freezing cycle and produced 10 eggs, 8 eggs were mature and frozen. When she present back 10 years later to utilize her eggs and thaw all of them 7 eggs are expected to survive, 6 eggs are expected to fertilize. If three embryos were transferred her chance for delivering a baby is 20% (the remaining three embryos are frozen). If The first cycle does not succeed and the next three embryos were transferred, her cumulative chance for having a baby from the original egg freezing cycle is approximately 40%.

Sorting through statistics of egg freezing is difficult. No single clinic can present convincing statistic due to small number of egg thaw and transfer (not just egg freezing cycles). Most studies present select donors and selected women and not directly applicable to everyone. And then there is the safety issue and lack of long term follow up data related to safety and health of newborns.

Age is most important predictive of success of egg freezing followed by method of freezing. Vitrification much better than older slow freezing methods. There is now reasonable body of data, though not definitive, that allows prediction of outcome for egg freezing using vitrification based on age and the

expected number of retrieved oocytes. It is neither accurate nor scientific to label egg freezing with terms such as reliable and guarantee. It certainly is not a guarantee of children. What is more productive is to i. try to avoid egg freezing through trying to conceive. If not possible, in a short while, then ii. understand your own personal chances of delivering a healthy baby through egg freezing and if they seem reasonable to you consider the procedure, taking in consideration the limitation of available data and filtering out the marketing hype.