Chennai Menopause Society

"Changes not Challenges"

Fertility & Aging

Healthy Aging - Series 6

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PRESIDENT'S NOTE

Dear Members

I would like to start by wishing you all good health.

As per our mission we have conducted Public Awareness Programme for Govt School teachers, along with Rotaract Guindy for their members and for employees of Ruhrpumpen Company.

In the month of June webinar was arranged on International yoga day.

Online Live yoga workshop by Mrs Sai Kripa and Mrs Durga was well appreciated by the delegates. Dr. Maninder Ahuja and Dr. Shobhana Mohandas were Guests of Honour.

In the month of July webinar was conducted on International Population day along with Tamil Nadu Women Doctor's Association. Prof. J. A. Jayalal IMA National President was our chief guest. Panel discussion moderated by Dr Nandita Thakkaron "Rights& Choices in Women's Journey" was enjoyable and informative

Chennai Menopause society along with Nellore Obstetrics Gynaec society conducted Webinar on "Way to Live with Menopause".

Short film on "Aging Gracefully" was release by Dr. Kani Mozhi. NVN Somu.

I thank all members for making our events a grand success.

Once again warm wishes to one and all and stay safe.

Dr. N. Hephziba Kirubamani

President, Chennai Menopause Society

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Article - 1

Paternal Ageing

Author: Dr. B. Kalpana

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The oldest age of paternity noted in a scientific publication was 94 years. Women experience an age-dependent increase in various adverse reproductive events such as infertility, pregnancy complications and perinatal maternal morbidity and mortality, as well as an impaired perinatal and post-natal outcome of the offspring. Although female fertility reaches a natural limit by the occurrence of menopause, male reproductive functions alter only slowly over a period of years and androgen production, spermatogenesis and sexual function are basically sustained lifelong, albeit with age dependent alterations. The production of reproductive hormones, sexual function, semen production, fertility, pregnancy outcome and the incidence of some birth defects and diseases in offspring are all linked to paternal age Increased concentration of follicle-stimulating hormone (FSH) in aged men has been linked to germ cell degeneration during meiosis, with a negative effect on daily sperm production. The impact of male age on histopathological aspects in the aging testes leads not only to reduced numbers of Sertoli cells, Leydig cells and germ cells, but also to other changes, as for example, thickening of the basal membrane of the tubuli seminiferi parallel to a reduction of the seminiferous epithelium and defective vascularization of the testicular parenchyma. The pathophysiological basis of age-impact on testes and semen parameters may be due to the specific effects of age alone, but can also be based on factors associated with age, as for example vascular diseases, obesity, infections of the accessory reproductive glands or an accumulation of toxic substances.

Semen volume and seminal fructose concentration decrease with age, possibly due to a seminal vesicle insufficiency, since the seminal vesicle contributes most to ejaculate volume Factors leading to decreased sperm motility could be found in altered functions of post-testicular glands such as the prostate and, more probable, the epididymis, as the swimming ability of spermatozoa is acquired during epididymal transit and motility is dependent on dilution into seminal plasma. Prostate- specific-antigen (PSA) and a-glucosidase, markers secreted by the prostate and the epididymis, respectively, decrease with age and are positively correlated to sperm motility. Age-dependent alterations of the epididymis might lead to disturbed mitochondrial functioning, as an important part of epididymal sperm maturation is the activation of sperm mitochondria. Which could by itself already be altered via genetic mechanisms, as highlighted below. Increase in the prevalence of infections in the accessory glands associated with significantly lower sperm counts. ROS levels show a significant, age-dependent increase in the aging male and may lead to DNA damage. high paternal age is an independent risk factors for miscarriage. Increased paternal age is associated with some chromosomal abnormalities in the spermatozoa and might thus play a role in the incidence of spontaneous miscarriages as well The overall risk for Caesarean delivery was twice as high in couples with the woman older than 35 and the man older than 40 years, compared with couples with both parents aged 20–29 years. paternal contributions to pre-eclampsia are clearly evident, and the only evaluation of paternal age effects shows a U-shaped increase of risk for pre-eclampsia with the highest risk in men aged 45 and older. Not only higher maternal age but also increasing paternal age (at least over 40 years) is associated with lower fertility, an increase in pregnancy-associated complications (as miscarriage rate, preeclampsia, possibly utero placental bleeding disorders, preterm births and surgical deliveries) and an increase in adverse outcome in the offspring. These associations are the reason why the age of semen donors is now limited to 40 or 45 years in some countries. Increasing paternal age can be associated with decreasing androgen levels, decreased sexual activity, alterations of testicular morphology and a deterioration of semen quality

(volume, motility, morphology). Increased paternal age has an influence on DNA integrity of sperm, increases telomere length in spermatozoa and is suggested to have epigenetic effects. These changes may, at least in part, be responsible for the association of paternal age over 40 years with reduced fertility, an increase in pregnancy-associated complications and adverse outcome in the offspring.

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Article - 2

Preimplantation Genetic Diagnosis

Author: Dr Kundan Ingale

Chairperson, Infertility Committee FOGSI 2020-24

Introduction

Preimplantation Genetic Diagnosis (PGD) is a testing modality to identify genetic alterations in embryos prior to implantation. According to ESHRE PGD consortium best practice guidelines, it is classified in two categories: high risk PGD & low risk PGD (PGS).

PGS is performed in couples who are at high risk of transmitting a genetic or chromosomal aberrations to their off-springs like inherited monogenic disorders which includes autosomal recessive disorders, autosomal dominant disorders, X-linked disorders or structural chromosomal aberrations. PGS is carried out for infertile patients to improve the pregnancy rate in women with advanced maternal age, repeated IVF failures & couples experienced repeated abortions with known cause and having normal karyotype. PGS is offered for selecting chromosomally normal embryos.

PGS involved formation of embryos through intra cytoplasmic sperm injection (ICSI), single cell biopsy of embryos followed by vitrification of embryos which are transferred in subsequent cycles.

Types of embryo biopsy for PGD:

1) **Polar body biopsy**: sequential methods involves first polar body removal from the oocyte on the day of oocyte retrieval between 36hrs and 42 hrs post HCG

injection. In fact both polar bodies can be removed simultaneously between 9hrs & 22 hrs post insemination.

2) **Blastomere biopsy**: Single blastomere is removed on day 3 of embryo development. Due to high chances of associated with mosaicism, it is not clinically beneficial. Correction of mosaicism is possible in culture till blastocysts, it is not popular for diagnosis of mosaicism.
3) **Day 5 Trophectoderm (TE) biopsy**: It is done on day 5 of embryo development. TE cells are removed after drilling of zone with Laser followed by herniation of TE. TE cells can be subjected for both PGT for aneuploidies(PGT-A) as well as for monogenic diseases(PGT-M)

First generation PGT involved genetic diagnosis by fluorescent in-situ hybridization (FISH) which had limitation of screening for only 5 chromosomes i.e. 13, 18, 21 & sex chromosomes. Second generation PGT involved comprehensive chromosomal screening (CCS). Array CGH required whole genome amplification and checking against control sample. Other CCS involved quantitative polymerase chain reaction (qPCR) and single nucleotide polymorphism (SNP) arrays which had drawbacks like very expensive & technically challenging.

Now a days NGS technology helps to detect all mosaicism and sub chromosomal segmental changes. It provides results in 24 hrs. It also helps to detect partial or segmental ploidies, unbalanced translocations. It is only technique which detects mosaicism. It is cost effective.

Fluorescent in-situ hybridization (FISH)

It is used for recognition of numerical and structural aberrations in the embryo. The biopsied cell is fixed onto the glass slide and hybridized to an in situ chromosomal target using fluorescently labeled DNA probe. Disadvantages associated with FISH are no hybridization, split signals, overlapping signals & limited to testing of a fixed number of chromosomes.

Polymerase chain reaction (PCR)

PCR is used for detection of single gene disorder & involved in vitro amplification of target DNA in the host cell genome resulting in a million fold copies of the target region which then subjected for analysis. One important precaution is required that we need to avoid contamination of host cell DNA. Sometimes allele drop out in amplification can create challenge.

Thalassemia screening by multiplex PCR

1) Presence of peak representing normal allele and absence of peak of mutant allele suggest normal pattern for thalassemia
2) Presence of peak of normal as well as mutant allele suggest β-thalassemia minor status
3) Presence of peak representing mutant allele and absence of peak of normal allele suggest β-thalassemia major status

Real Time quantitative PCR (RT-qPCR)

It is PCR based assay which identifies whole chromosome aneuploidy. It detects increase (trisomy) or decrease (monosomy) number of chromosomes.

Comparative genomic hybridization (CGH)

It is a ratio labelling protocol where the testing sample is tagged with fluorescent dye (green) and it is compared with normal reference male or female genome, tagged with red dye. The CGH chips have 4000 markers throughout genome.

Single nucleotide Polymorphism (SNP)

It involved analysis of 3, 00,000 SNPs spaced throughout the genome, located on non-exon segment of genome. It provides genotype of tasting sample and then it is compared with human Hapmap reference genome. This is used to identify whole chromosome

aneuploidy and also identify 250 common structural chromosome aberrations throughout genome.

Next generation sequencing (NGS)

NGS involves optimized DNA amplification to reduce artifacts during amplification process. After DNA amplification, barcoding step follows to allow the identification of embryo specific sequences. It is then broken down into small sequence ready fragments which are subjected to massively parallel sequencing.

Indications for PGD

1) For couples who were at risk of transmitting the genetic abnormality
2) For couples who were carriers of a balanced carrier
3) To improve IVF outcomes in cases like advanced maternal age, recurrent pregnancy loss and recurrent implantation failures.

PGT-A can be offered to women under 35yrs as they produce several blastocysts as one third of blasts from young women show high aneuploidy.

Concerns regarding PGD

2-10 TE cells which are retrieved for sampling can represent the genetic status of inner cell mass.

Embryo biopsy can have detrimental effect on embryo especially in low quality blastocyst.

Ethical and social aspects

Misuse of advanced technology and not regularized in many countries has raised ethical and social aspects for PGD. As it involves embryo manipulation, unnecessary utilization of resources, propagation of eugenics and protection of rights of unborn child, many issues are raised for judicious use of PGD.

Summary

PGS is proved to be very useful technology for couples who are either carrier of genetic disease or experiencing recurrent abortions or implantation failures. PGS demands highly skilled molecular biologists, fully equipped molecular biology laboratory and close collaboration between clinical genetists and fertility specialists. Use of vitrification and cryopreservation protocols helped us to freeze embryo post biopsy and transfer in a subsequent cycle. Like any new technology this technology also needs to be regularized and to be used for betterment of the society and mankind.

Article - 3

Egg Freezing - Is it RIGHT to freeze time!!!

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India is a country which has faced the brunt of changing social values, war between generations and induced western dreamy aspirations! However, our core values till date remains undeterred. Hence, we find it a challenge to welcome and readily accept anything that is against Nature or Tradition. We do feel justified at the end of the day because when an ethical battle happens, we are always on the right side!

Women are born with a finite number of egg reserve, thus the best fertility potential is between 19-25 years of age .Traditionally, this was the most desired age of marriage by all Indian brides. Soon, literate and career oriented women competed at par with men .Most were successful at multitasking handling role of a mother and working woman with help and support from friends and family. In modern times, when women's empowerment has different interpretations, moving away from the traditional bondage shackles is considered the only way forward . Singularly fierceful woman to complete education, training, professional competency and achieve her goals, definitely loses to time to start a family! Then came the awareness that togetherness and joint family values has its advantages but it's too late!

Cryopreservation is a revolution where in eggs ,sperms and embryos can be preserved for future use .Dr Christopher Chen of Singapore reported the world's first pregnancy in 1986 using previously frozen oocytes. Dr. Lilia Kuleshova was the first scientist to achieve verification of human oocytes that resulted in a live birth in 1999.Vitrification took it a

step further as it was faster and easier and safer technique for the embryologist. In October 2012 when the American Society for Reproductive Medicine (ASRM) lifted the 'experimental' label from the process,social egg freezing parties by companies brought in the concept -lets freeze biological age till you find the romantic partner!

Oocyte verification became an accepted procedure to benefit those who were afflicted by cancer or benign endometriosis .Medical reasons are primarily cancer patients who survive longer and desire a better quality of life .Oncotherapy led to an iatrogenic gonadal loss, be it surgical, chemo or radiotherapy , they all have detrimental consequences on male and female fertility potential. No non co-conditions where cryopreservation remains a fertility rescue include autoimmune diseases, myelodysplastic syndromes, germ cell degeneration affected by premature ovarian failure (POF) based on idiopathic or genetic origin as in Turner syndrome mosaicism, X trisomy, and X-fragile syndrome. Egg freezing is a novel techno-medical innovation getting commercialized for non-medical reasons to healthy, fertile women, who wished to postpone motherhood for various reasons.

Social egg freezing became popular because of media publicity and a career gimmick by mighty Facebook. In 2014, Facebook and Apple made headlines by offering to give female employees $20,000 of egg-freezing benefits as a nudge policy to encourage people to choose career over family! This medical innovation is being widely promoted by private fertility centers and the lay press throughout the world, leading to mixed public reaction.

Today's woman from smartphone era tries to control time hence the option of social egg freezing appears to be attractive! She can decide her timeline by freezing her eggs on time and choose to find her partner in leisure and start a family when she believes she is ready. Now we wonder if it is the proper solution to the problem or is it creating further challenges like distorting health economics, managing the storage of cryopreserved oocytes , supporting the legality of egg banks and the possibility that egg freezing will play a role in enabling childbearing for gays, lesbians, and unmarried persons. What

about the ethical aspects -the rights of the unborn child! Social freezing means egg storing of a healthy, fertile woman, in order to have a pregnancy later in her life, *i.e.* at the age of 45 to 50,it should ideally be performed on women around 25 years of age in order to increase their chances of a future pregnancy, but, in reality, it is mostly performed after the age of 35. Social egg freezing is by no means a *social* activity as there are no other people involved apart from the woman herself. The act would only be social if the woman determines that if she does not need her frozen oocytes and decides to donate them to another woman.

In case of assisted reproductive techniques, the pregnancy rate per embryo transfer for women receiving IVF treatment using their own fresh eggs drops between the ages of 35 and 45 from 38.2% to 2.2%.For women freezing their eggs in their mid-20s to mid-30s, there is a clinical pregnancy rate per thawed oocyte of between 4.5% and 12%. Today, pregnancy rates for IVF using frozen oocytes are now broadly comparable with pregnancy rates using fresh oocytes, so that a woman who froze her eggs at the age of 35or less could benefit from an IVF success rate closer to 38% than 2% well into her 40s.So freezing age matters ,the younger the better .We must understand every new technology must be weighed with evidence and policy makers have to do their health economics analysis whether it can become part of mainstream practice .When funding becomes an insurance based issue in fertility treatment ,the added costs to the woman might be overwhelming, ovarian stimulation and oocyte retrieval are uncomfortable procedures that women will only undertake if they are convinced that they will actually benefit from the procedure !

Elective oocyte freezing consists of two separate steps that are clearly distinct in time: first, ovarian stimulation, oocyte retrieval, cryopreservation and storage that we identify in the oocyte banking; and second, even several years later, thawing and fertilization of the cryopreserved oocytes. From a medical point of view, we have to consider the balance between the risks of the procedures (ovarian hyper stimulation, oocyte pick up and pregnancy) and the benefits, for the mother and the child. In an ethical perspective, we

should also consider the risks for the future child: due to advanced maternal age and pregnancy complications, neonatal complications are also increased, comprising prematurity and lower mean birth weights ,and handling high risk pregnancy becomes an expensive multi disciplinary team effort.

Egg banks have their own problems – unused Self frozen eggs due to a myriad of reasons: women may have completed their family through natural conception or may have passed away or break up with their partner or may have abandoned their desire to have children .The potential donors need to overcome a double threshold: the first with regard to the physically demanding procedures of ovarian stimulation and oocyte retrieval; secondly, with regard to the psychological burden of becoming the genetic parent of a child that one does not know.

Donors may receive a personal benefit, either cash or in kind (in oocyte sharing schemes).

Egg banking also provides the possibility to quarantine oocytes for 6 months or longer to retest donors for safer donation, as is the criteria established for semen banks.

Furthermore, young people are not aware of the natural limits of age related human fertility, with increasing maternal age comes increasing risks of miscarriage and obstetrical/neonatal complications hence its essential to plan their reproductive choices more realistically, thus reducing the chance of involuntary childlessness. The need for the reproductive health education at school and college level by the policy makers .While we are clear egg freezing is a boon for medical reasons we are speculating that elective freezing maybe a bane for non medical reasons. We live in an era where commercialization of medicine has become inevitable but it is always your choice how you want to practice!

Article – 4

ART at Forty

Author: Dr Jayarani Kamaraj

Akash Fertility Centre

How old is too old for assisted reproductive technology?

The Challenge of Pregnancy over 40: Modern medicine is already allowing women to have children far later in life than their ancestors, but how far can female fertility really be extended? **For 40 year and above women, trying to get pregnant could be a challenge. Statistics show that up to 15% of couples struggle with infertility. Most cases happen with men and women over 40 since fertility declines significantly with age. A woman's ovarian reserve lowers considerably at this stage, and some men may have poor sperm quality. Today, infertility is no longer an ultimatum thanks to techniques like in vitro fertilization or IVF. However, some people over 40 can consider IUI first before moving to IVF.**

"It's one of nature's great inequities," says Dagan Wells, professor of reproductive medicine at the University of Oxford. He is referring to the progressive, and largely irreversible, decline in female fertility from the age of 35 years onwards.

Men also experience a decline in their baby-making ability as they get older, but this fall in fertility tends to start later and occur much more slowly than in women. The fertility rate for men tends to begin falling around the age of 40-45 years old.

But when exactly does a woman's fertility start declining? And when does that decline result in the end of natural fertility?

For millennia, women have been getting pregnant and bearing children in their teens and early 20s – not much different from the Krapina Neanderthals, living in Northern Croatia 30,000 years ago, whose fossilised remains suggest gave birth to their first child at 15 years of age. Prior to the 1960s, women in the US were having their first child on average at around the age of 21.

In 2017, however, the average age of mothers giving birth in all OECD countries was 30. Just under half (44%) of all live births in England and Wales in the same year were to mothers aged 30 while the average age of women giving birth to their first child in South Korea was 31.

But what does this mean in the context of the ticking clock of female fertility?

Numbers matter

For decades, scientists have associated the decline in female fertility with the age-related decrease in the number of eggs contained within a woman's ovaries. Each, if fertilised, has the potential to grow into a baby.

Unlike men, whose reproductive organs produce millions of fresh sperm on a daily basis, women are born with all the eggs that they will ever possess. Moreover, this number steadily declines as a woman ages: from one million eggs at birth to 300,000 by puberty, 25,000 by the age of 37 and 1,000 by the age of 51. Of all these, however, just 300 to 400 eggs with baby-making-potential – normally just one a month – will mature and eventually be released from a woman's ovaries through ovulation across her entire life. For reasons not yet fully understood, the rest undergo a natural process of degeneration and will never be ovulated.

While egg counts decline as women age, so does the quality of the chromosomes and the DNA contained within each egg

Most girls begin menstruating between nine and 13 years of age, but their ovaries don't start releasing eggs until a least a year or two later. Simple mathematics would suggest a woman's egg supply would then typically exhaust itself around 33 years later. And in most women, fertility does indeed tend to cease up to eight years before the onset of menopause, which for American women is around the time of their 51st birthday.

While such crude calculations do not take the natural variability that can exist between women into account, or the time windows during which ovaries might release more than one egg in a month, or months in which no egg is released at all, they can give a rough estimate of just how long the female fertility timeline can be.

A more precise estimate of a woman's egg count, also known as "ovarian reserve", can be obtained by measuring the level of hormone called anti-Mullerian hormone (AMH) in a woman's blood. We now know that AMH, produced by the ovaries of fertile, adult women, plays a vital role in the metamorphosis of an immature egg cell into a mature, hopeful egg, complete with all the biological prerequisites to create a healthy baby. Better functioning ovaries, with larger egg stores, produce more AMH. Levels of the hormone decline as the timeline of female fertility progresses – average levels in 30 to 35 year olds are roughly two-thirds that of younger women while levels in women aged over 45 years are a quarter of those seen in women in their 20s.

Andrea Jurisicova, an embryologist at the Lunenfeld-Tanenbaum Research Institute of Mount Sinai Hospital, has spent years studying the mechanisms that underpin the decline in female fertility with age, and investigating what can be done to slow this. Her research has found that ovarian reserve is genetically regulated but that a woman's life experiences – such as stress, exposure to radiation or toxic chemicals and even those from when she herself was in the womb – determine egg numbers in later life.

Quality matters

But female fertility isn't just about the quantity of eggs. Quality matters too, and is much more technically challenging to assess than egg numbers. While egg counts decline as women age, so does the quality of the chromosomes and the DNA contained within each egg.

"Chromosomal abnormalities in human eggs are extremely common," says Wells. "It's not something that should be considered to be a particularly abnormal situation, and in most cases its something that all women, even young women, will have in their eggs at a low level but that level increases with advancing age."

For a woman in her 20s, a quarter of her eggs may be expected to have chromosomal abnormalities – this increases to up to 40% for a woman between 30 and 35, and "goes up simply exponentially from there on". Beyond the age of 35, the frequency of these chromosomally abnormal eggs increases by 0.5% per month, so that for a woman in her early 40s up to three-quarters of her eggs will have chromosomal abnormalities.

An egg with too many or too few chromosomes, broken or damaged chromosomes will often fail to develop properly

Having chromosomal abnormalities in her eggs doesn't necessarily mean a woman is infertile, but they do mean that more of her menstrual cycles will produce eggs that are less likely to produce a viable baby.

Chromosomes are bundles of tightly coiled DNA that hold the genetic information needed for an organism to develop. A human egg contains 23 chromosomes – the half of your genetic code that comes from your mother – which needs to combine with the 23 chromosomes from your father's sperm to develop into a viable embryo. An egg with too many or too few chromosomes, broken or damaged chromosomes will often fail to develop properly. In some cases a baby can still be born with chromosomal abnormalities, as happens with Down's Syndrome.

But most chromosomal abnormalities tend to be lethal to the extremely young embryo, resulting in the embryo failing to implant in the lining of the womb or a very early miscarriage, often between five and eight weeks of pregnancy.

While the risk of chromosomal abnormalities is known to be higher in the eggs of older women, a recent European study found that the level of chromosomal abnormalities is also high in younger women too – from 13 into their early 20s. The findings suggest that female fertility timeline follows a n-shaped pattern, with peak fertility observed in the mid-20s and lower levels of fertility both in very young and older women.

Elsewhere in the egg, faulty mitochondria – the tiny power stations that provide energy for our cells and which we all inherit from our mothers – can also be a problem in older women. Studies have shown that up to half the eggs of women who are older than 35 carry mutations in their mitochondrial DNA, compared to a third of the eggs in younger women.

"An egg needs a threshold of about 40,000 mitochondrial DNA copies to make an embryo," says Jurisicova.

For Wells, the evidence is clear.

"The rate of decline accelerates around the age of 35 and the vast majority of women are essentially infertile by the time they reach 45," says Wells. "Importantly, this is years, maybe even a decade, before menopause. Everyone expects to be a little less fertile when you are older, but the extent of that decline takes a lot of people by surprise."

It would be wrong to focus only on female fertility. Some studies have shown that sperm quality also declines with age in men, starting in their 20s. Sperm mobility – the ability of it to swim around – has been found to decline by around 0.7% every year while the sperm of older men carry more mutations in their DNA. Older fathers also pass on more mutations to their children than mothers do from their eggs.

Best egg

"The human egg is a remarkable and unusual cell, it's the biggest cell in the body, and has a unique feature," says Wells. He is referring to the egg's ability to stop halfway through its growth and remain in a state of suspended animation for years, even decades, until it is eventually ovulated. His research suggests that it is the egg's ability to hold its chromosomes in a stable configuration during this period of hibernation that governs its ability to make an embryo and a baby.

While there may be little that science can do to change the number of eggs a woman will have during her life, there are ways to improve egg quality

Jurisicova's work adds another piece to the puzzle. Her work suggests that human eggs undergo a process of growth and maturation within the ovary for at least nine months before they are released during ovulation. "The quality of the egg released is the culmination of all the health and environmental influences on that growing egg over the past nine months," she says. Stress, exposure to radiation or toxic chemicals during this time can have an adverse effects on the developing egg.

It is perhaps interesting that the duration of this incubation period – from when an egg emerges from hibernation and begins developing – uncannily resembles the number of months a baby spends within the womb before it is born. During this period of maturation, the egg develops the resources it will need should it be fertilised.

"The egg has to be extremely well resourced," says Wells. "For the first three days following fertilisation the embryo doesn't really make anything for itself – it doesn't transcribe its genes, it doesn't make proteins – its completely reliant on what the egg has provided for it. A more mature egg is more likely to be better resourced than a less mature one."

While there may be little that science can do to change the number of eggs that nature (or genetics) decides a woman will have during her life, Wells and Jurisicova agree there are

ways to improve, or rescue, egg quality. Adopting a healthy lifestyle, exercising regularly, reducing stress and making sure that health problems such as hypothyroidism and other autoimmune conditions are well controlled can all help.

Jurisicova recently found that giving female mice the antioxidant coenzyme Q10 delivers promising results – the mice that received the supplement produced better quality eggs with more properly aligned chromosomes and better mitochondrial function. They were also more successful in producing live babies, than the mice that did not receive the supplements. The results are, however, yet to be replicated in humans.

Can age impact IUI?

IUI has a 10-20% success rate after 2-3 cycles. This may look like a low figure, but a healthy woman has a 20% chance of getting pregnant each month at age 30. From age 40, this figure decreases significantly, and IUI is no different. For instance, IUI for women between the ages of 40-42 has a 9.8% success rate. The reduced success rates are often due to the diminished ovarian reserve. Even with a low figure, IUI can still be a viable option before IVF. If the woman has a healthy uterus, but there are some male-factor infertility concerns, IUI may be a good option. IUI is also cheaper and less stressful on the body. So opting for a few cycles of IUI first can be sufficient.

When to consider IVF

There are times when patients are likely to have better results by avoiding IUI and opting for IVF. Hopeful parents should consider IVF if there are clear reproductive conditions like fallopian tube damage or endometriosis. IVF also works well for women with a significantly diminished ovarian reserve. Aside from female infertility, severe male infertility may require advanced techniques such as intracytoplasmic sperm injection (ICSI).

Age 40 and above is a very delicate time for fertility. The odds of getting pregnant decline significantly, but techniques like IUI and IVF can help. IVF has higher success rates than IUI. However, that does not mean IUI won't work at all. Women over 40 with a healthy reproductive organ can try IUI first. If there are conditions like PCOS, cervical mucus, or male-factor infertility, IUI can also help. IVF can help with severe reproductive concerns or unexplained infertility.

The journey, not the destination

Mothers don't just need to contend with their fertility as they get older, but also greater risks during pregnancy, labour and delivery. The First and Second Trimester Evaluation of Risk (Faster) trial, a US study funded by the US National Institute of Child Health and Human Development (NICHD), looked at the health records of over 36,000 women. They found mothers over 40 were two to three times more likely to experience health problems during pregnancy including diabetes and high blood pressure. They were twice as likely to experience bleeding from their placentas, have a caesarean delivery and to lose their baby later on in pregnancy.

The children of older first-time mothers who are 40 years and above also have an increased risk of health problems at birth, such as low birth weight and congenital abnormalities. They also have a 50% increased risk of being born preterm and, perhaps consequently, are at increased risk of requiring neonatal intensive care after birth.

But this is still only one half of the equation. Older fathers also bring additional health risks for their children. Babies with older fathers are more likely to be born prematurely, have a lower birth weight and higher risk of seizures. Some studies have also linked increasing paternal age to a greater risk of conditions such as autism and ADHD where the father is over the age of 40, but the evidence remains inconsistent.

Is it possible to extend female fertility and for how long? As is often the case, where nature creates inequity, science attempts to level the playing field. In September last year,

Erramatti Mangamma, a 74-year-old from southern India become the world's oldest first-time mother, delivering twin baby girls conceived via In Vitro Fertilization (IVF) after 57 years of infertility. Three years ago, 72-year-old Daljinder Kaur, from north India, gave birth to a son after nearly five decades of marriage and two unsuccessful IVF attempts.

The significant advances in reproductive medicine over the past decades have greatly increased the safety, success, accessibility and affordability of artificial reproductive techniques. Approximately 230 babies are born in the UK each year to women aged 50 and over while 9% of all first-time mothers in the US were aged above 35 in 2014.

But as we have seen, these techniques are still limited to a degree by the age of the egg. This is, not least, because of the effects of ageing on the DNA, but also because older eggs have been exposed to environmental toxins for a longer amount of time. It is possible, of course, for women to undergo IVF using a donated egg from a younger woman. Nearly all fertility clinics across the world now also offer women an option to store their eggs, frozen in time, until she is ready for them to be thawed, fertilised and transplanted into her womb.

"The difficulties experienced with older women trying to have children is not related to the uterus but to the egg, and chromosomal abnormalities are at the heart of that," says Wells. "The egg is the seed rather than the soil. Many of the very early steps in human development are determined by what the egg provides."

With the help of technologies like pre-implantation genetic testing, Wells and his fellow embryologists are developing ways of identifying the best eggs that can be used in IVF treatments. Other techniques such as mitochondrial replacement therapy are also helping mothers with defects in their eggs give birth to healthy children.

But while science is making commendable steps to help prolong the ticking clock of female fertility, it may not ever be possible to keep it going indefinitely. The decline of natural female fertility is as inevitable as it is universal.

Health Matters - Sleep

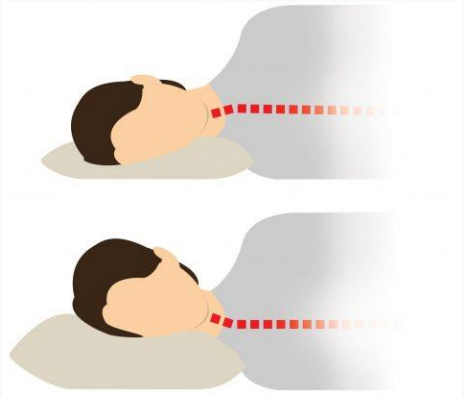
Do you value sleep as much as you value your work?

Sleep deprivation causes daytime fatigue, inability to focus, irritability. In the longterm,it also causes obesity, psychological disturbances and increases the risk of cardiovascular diseases.

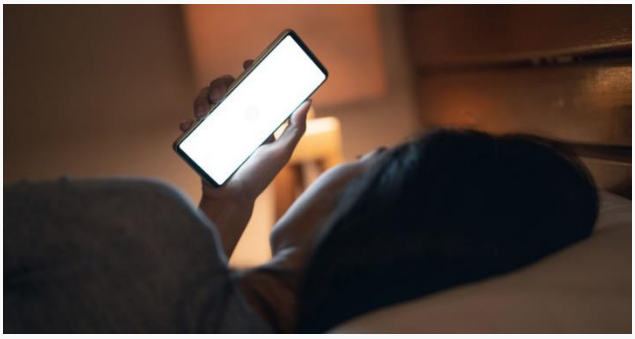
Consider sleep a priority and an important component of your health and wellbeing.

Wake(5% of the night) Everybody has moments during the night when they wake up. Most of the time, these waking period are short and forgettable, but sometimes having too many waking moments can interrupt your rest	REM (20% of the night) This is when you tend to dream. You tend to have very high brain activity during this time
Light sleep (55% of the time) This is the bulk of our sleep time. Your body is relaxed, there is very little brain activity, and it is easy to wake up. This is the ideal time in your sleep cycle to wake up feeling refreshed.	Deep Sleep (20% of the night) This is the time when our minds and bodies get rejuvenated. Your body is relaxed, and it is very hard to wake up from this stage of sleep.

Common mistakes about sleep



Pillow being too thick (high) or too thin (low)



Watching electronic screens in bed

Rooms with the same brightness during the day and the night are a hazard. Dark in the room during the night and wake up in bright sunlight. This will synchronise with melatonin secretion in the body.

If you find it difficult to fall asleep, the following induction techniques may be useful.

Mild stretching/ yoga/ meditation	Natural drinks that help in relaxation/ aromatherapy
Hypnotherapy/ relaxation techniques	Smart phone apps that aid in sleep

Chennai Menopause Society

"Changes not Challenges"

Fertility & Aging (Healthy Aging - Series 6)

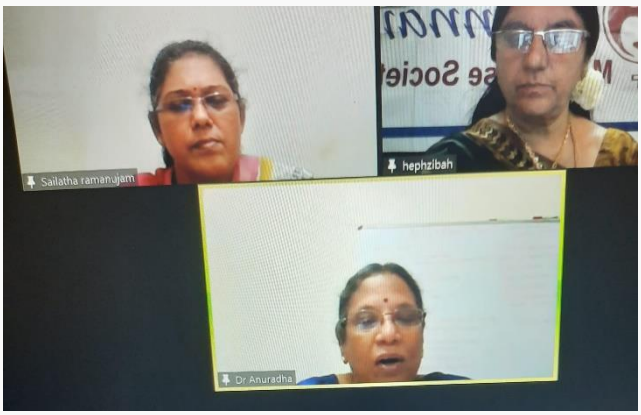
Chennai Menopause Society

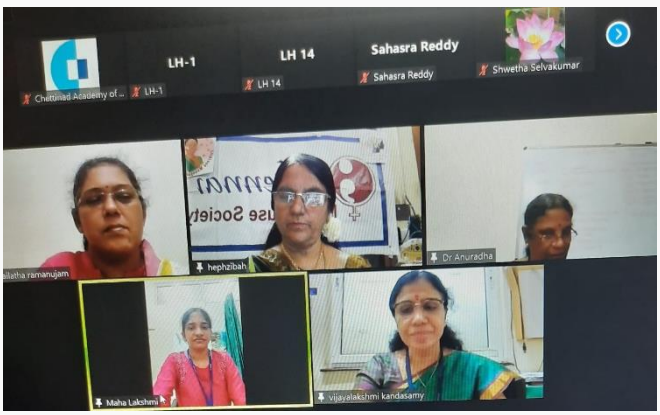
Embrace Menopause With Grace

Chennai Menopause Society Past Events

Chennai Menopause Society & TOGS Program

Chennai Menopause Society & Chettinadu Medical College Awareness programme for MBBS students



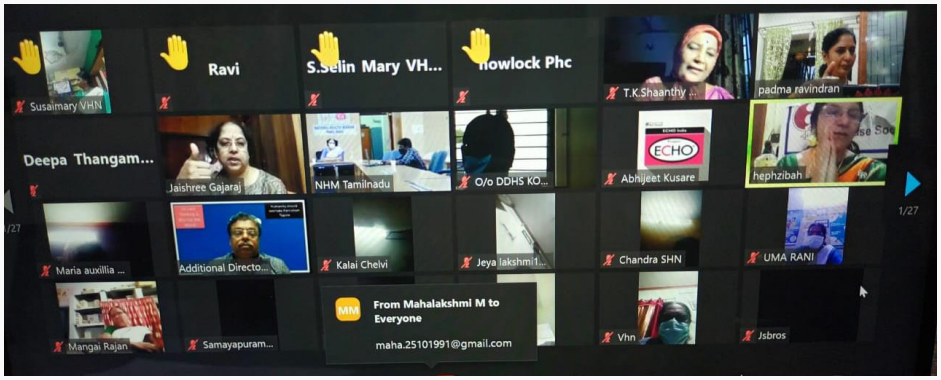


Chennai Menopause Society

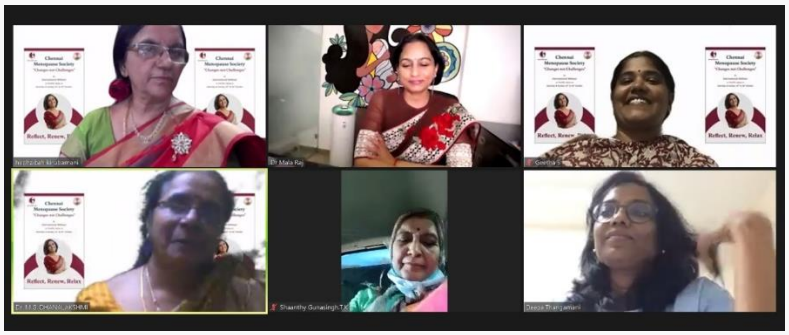
"Changes not Challenges"

Fertility & Aging (Healthy Aging - Series 6)

Awareness programme for 1000 PHC Doctors



International webinar on 23rd 24th on Healthy aging



There is no more creative force in the world than the menopausal woman with Zest

The most important thing is growing old gracefully

The best part of the art of living is to know to grow old gracefully