KERALA FEDERATION OF OBSTETRICS & GYNECOLOGY

KFOG JOURNAL

MENOPAUSE

November- December | 2021 VOL: 15, No:3

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Dr. Ajith S.
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President KFOG

Respected seniors and dear friends

It is heartening to see Dr. Suchithra and team regularly bringing out issues of our journal despite current covid situation. The topic for the current issue is "Menopause", with special emphasis on the mental health aspect, in tune with our theme "Minding the mind". I thank Dr. Acka Priya Varghese associate editor, Dr. V. Rajasekharan Nair Sir, the patron and all the authors for their invaluable contribution in bringing out this issue.

Menopause is a varied experience for every woman. Women should be provided with clear evidence-based information on menopause to break free from confusion over menopausal symptoms. With increasing life expectancy many women are bound to live one third to half of their life in post-menopausal phase. The menopausal symptoms can have a major impact on their health, work relationships and quality of life. I hope this issue of KFOG journal will help our members understand management of menopause better, thereby helping them to alleviate the problems of menopausal women in our society.

I request all of you to use our updated KFOG website.

With warm regards

Dr. Ajith S. MD, FRCOG
President KFOG

Dr. Venugopal M .
Secretary KFOG

SECRETARY'S MESSAGE

Dear KFOGites,

Hope all of you are in good health, at a time, when the world is getting rid of the shackles imposed by the pandemic.

In spite of all adversities, it is heartening to note that our KFOG bulletin is coming out on time.

This edition of KFOG bulletin has some varied contributions, focused on Menopause. Dr. Suchitra and team, along with Dr. Acka Priya, have taken a lot of effort in compiling the articles, which are very important in our daily practice.

Congratulations to each one who contributed to this edition of the bulletin.

The bulletin showcases the energy and enthusiasm of our members and the attempt to give an opportunity to new faces in KFOG is laudable.

I urge all members to enthusiastically contribute to the future editions of the publication, because creativity always brings positive energy.

During the pandemic, the bulletin has played an important role in keeping our members updated and I am sure it will continue to do so in the future.

Best wishes to all and your families as we are waiting to usher in 2022. Let us all hope for the best.

Dr. Venugopal M.
Secretary KFOG

FOREWORD

Dr. V. Rajasekharan Nair, MD, DGO
Head of Department, Obstetrics & Gynaecology, S.U.T. Hospital, Pattom, Trivandrum
Former President of KFOG

Menopause
"The wicked elder sister of Puberty"

Menopause is an inevitable biological transition which every woman has to undergo, when she has to surrender to the aging process. Increasing life expectancy has reoriented the menopause as a midlife phenomenon rather than a terminal old age event. Thus, a post menopausal woman should not be portrayed as somebody with decaying bone, clogged arteries, sexually impotent, quarrelsome lady who undergoes a battery of tests annually but should tempt us to view her holistically.

Probably the most common and distressing symptom of menopause is the hot flushes and night sweats.By making her understand the physiology behind it, women can easily cope with it. The most serious aftermath will be osteoporosis. By adopting an active healthy lifestyle, with dietary readjustments and calcium supplements, one can prevent fractures. Suitable life style and dietary modifications can thwart the coronary artery risks. Cancer risk can also be reduced by periodic check-ups. Andropause, the male counterpart of menopause, is more insidious in onset. When counselling menopausal women on sex life, this aspect of her partner also should be given attention. Keeping one physically and intellectually engaged may be the secret in managing menopausal problems successfully.

Hence Let us keep up a holistic view on menopause, consider it as positive phase of woman's life like puberty. I feel it is better to consider Menopause as the elder wicked sister of Puberty.

Thus the topic selected for the autumn issue of the KFOG journal 'Menopause' is indeed relevant. I congratulate the entire team of journal committee of the KFOG and the authors for bringing out this third issue of the KFOG journal.

EDITORS DESK

Dear Friends,

Greetings!!
Welcome to our third journal based on the topic Menopause. This, the time of a pause in a woman's life, when she wonders whether her femininity is waning, her bones start to creak and the fear of many lifestyle diseases, including cancer, begins to haunt her.... A time when her mind is adjusting to the 'empty nest' syndrome.... fluttering as her bodily changes make her anxious and depressed...

All these aspects are discussed by authors from Kochi, Kottayam, Alappuzha and Angamaly. They will be dissected by experts from all over India during the journal event on December 15th.

We are grateful to our Senior Professor Dr. Rajasekharan Nair for being our Patron for this issue.

Unstinting support from KFOG President Dr Ajith and Secretary Dr. Venugopal made this possible.

Most of all, my sincere appreciation to Associate Editor Dr. Acka Priya Varghese for expertly coordinating and creating this marvellous journal. A big hats-off to her and all the authors.

Now, let's enjoy reading and mulling over these informative and interesting articles!

Dr. Suchitra Sudhir
Editor, KFOG Journal 2021

Dear seniors and friends,

Warm greetings to you all. This is the third issue of the KFOG journal of 2021 which aims to cover the topic Menopause by the members of Alappuzha, Angamaly, Kochi and Kottayam OBG societies.

It has been a great blessing to work under the patronage of my own teacher Dr.V. Rajasekharan Nair.

I sincerely appreciate each one of the authors for their painstaking effort in making this journal a reality.

I am using this opportunity to express my thanks to the KFOG office bearers and senior members of KFOG for allowing me to partake in this prestigious activity.

I express my heart-felt gratitude to Dr. Suchitra Sudhir, the editor of the journal, for her encouragement and immense help.

Happy reading.

Dr. Acka Priya Varghese
Associate Editor,
KFOG Journal Third Issue 2021

HORMONE THERAPY-
The Right one for You

Women have menopause at a mean age of 51 years with 95 % of them having it between 45 to 55 years (1). If menopause occurs before the age of 40 years, is called Premature Ovarian Insufficiency (POI). The menopausal symptoms affects quality of life of a symptomatic woman. The symptom complex of menopause can be divided into Vasomotor symptoms (VMS), Somatic symptoms, Genitourinary Syndrome of Menopause (GSM), and

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Neuropsychiatric symptom. Vasomotor symptoms (hot flashes) is the most common symptom with approximately 85 percent of women, experiencing it. The majority of women with moderate to severe symptoms have a negative impact on sleep and quality of life. GSM is approximately seen in 50% of women, who develop symptoms and signs of estrogen deficiency changes on labia, vagina, urethra, and bladder. They have genital dryness, burning, and irritation; sexual symptoms of diminished lubrication and dyspareunia (2); and urinary symptoms of urgency, dysuria, and recurrent urinary tract infections.

Menopausal Hormone Therapy

Menopausal hormone therapy (MHT) describes both unopposed estrogen use for women who have undergone hysterectomy, and combined estrogen-progestin therapy (EPT) for women with an intact uterus. The use of hormone therapy (HT) is considered for different populations of women, including those with, surgical menopause, early and late menopause with symptoms, and primary ovarian insufficiency (POI) (3)

Prior to the Women's Health Initiative (WHI) trial results in 2002, HT was generally accepted as appropriate and safe for treatment of menopausal symptoms. The findings of the WHI, which raised concerns about breast cancer and CVD risk led many to stop prescribing HT. But subsequent randomized controlled trials such as the Kronos Early Estrogen Prevention Study (KEEPS) and the Early Versus Late Intervention Trial with Estradiol (ELITE) have continued to demonstrate a favorable safety profile of HT when started early in menopause (4).

Options Available

The options available include Estrogens, Estrogen and Progestin combinations, Progestin alone, SERMS, Tibolone and Testosterone therapy.

Estrogen Preparations available are given in Table 1. The contraindications and side effects are in Table2

TABLE 1

Preparations	Route	Dose	Current approach Low dose
1.Estrogens 17-beta estradiol	Oral	1 mg/day	0.5 mg/day
2.Transdermal Estrogen	Transdermal	0.05mg/day	0.25 mg
3.Conjugated Ethinyl Estrogen(CEE)	Oral	0.3 mg, 0.45 mg, 0.625 mg, 0.9 mg, and 1.25 mg	0.3 mg, 0.45 mg, 0.625 mg.
4.CEE	Cream	0.625mg/day	
5.Estrodiol	Vaginal ring	2mg	

TABLE 2

Contraindications- Oral Estradiol	Side effects	
Avoid in women with • hypertriglyceridemia, • active gallbladder disease, • known thrombophilias such as factor V Leiden • with history of venous thromboembolism [VTE].	• vaginal bleeding • breast tenderness • effects on coagulation • effects on inflammatory markers, • stroke	**Side effects low with low dosage**

2. Progestins

All women with an intact uterus need a progestin to be added to their estrogen to prevent endometrial hyperplasia, which can occur after as little as six months of unopposed estrogen. Women who have undergone hysterectomy should **not** receive a progestin. The available progestins are listed with their route, dose and side effects in Table 3.

TABLE 3

Preparations

Preparation	Route	Dose	Side effects
1. Micronised Progestogen	Oral	200mg daily x 12 days or 100mg daily continuously	Breast soreness Mood symptoms Bloating Vaginal bleeding Monthly bleeding in cyclic progesterone
2. Micronised Progestogen	Vaginally	100 mg daily	
3. Medroxy Progesterone acetate(MPA)	Oral	2.5 mg daily	
4. Progesterone inserts	Vaginal	100 mg	
5. Progestogen gel	Vaginal	4%	
6. LNG IUD	IUD	20 microgram / day	

3 Tissue Selective Estrogen Complex (TSEC)): Conjugated estrogen/ Bazedoxifene

This is the combination of Bazedoxifene, a selective estrogen receptor modulator (SERM), with conjugated estrogen (20 / 0.45 mg od orally). This product is for the treatment of menopausal vasomotor symptoms and osteoporosis prevention. Bazedoxifene prevents estrogen-induced endometrial hyperplasia. Potential candidates include women with moderate-to-severe hot flashes who have breast tenderness with standard EPT or women who cannot tolerate any type of progestin therapy. Like other SERMs, the risk of VTE is increased with Bazedoxifene (1).

4. Tibolone

Tibolone is a synthetic steroid whose

metabolites have estrogenic, androgenic and progestogenic properties. Dose is 2.5 mg / day orally. Tibolone reduces vasomotor symptoms when compared with placebo, but it is less effective than estrogen therapy. It also has a beneficial effect on bone mineral density.

The Long-term Intervention on Fracture with Tibolone (LIFT) trial, showed excess risk of stroke in women receiving Tibolone. Tibolone does not appear to increase mammographic density or the frequency of abnormal mammograms. No excess risk of breast cancer was seen. But in women with a personal history of breast cancer, use is associated with an increased risk (LIBERATE) trial). Based on the data, Tibolone should not be used in women with a history of breast cancer (1).

Testosterone therapy

May improve female sexual function in selected populations.

Examinations required prior to receiving MHT

Proper history taking, physical examination, and examinations for liver function, kidney function, anemia, fasting blood sugar, and blood tests of serum lipid profile, followed by mammography, BMD test, and Pap smear screening.

Thyroid function test, breast ultrasonography, and endometrial biopsy is done according to individual risk factors (5).

Clinical indications

Vasomotor symptom is the most common indication, for which HT remains the gold standard for relief. Other symptoms that respond to estrogen include sleep disturbances, depression, anxiety, and in some cases, joint aches and pains.

- Estrogen-alone therapy can be used for symptomatic women after hysterectomy.
- For symptomatic women with a uterus, combination therapy protects against endometrial neoplasia, either with a Progestin or Bazedoxifene.
- Micronized progesterone 300 mg nightly significantly decreases VMS (3).

The genitourinary syndrome of menopause (GSM)

HT is the most effective treatment for GSM.

- Low-dose topical vaginal estrogen preparations are effective and safer, with minimal systemic absorption.
- Low-dose vaginal estrogen should be used rather than systemic estrogen
- Includes creams, tablets, and rings containing estradiol or CEE
- Non-estrogen therapies include Ospemifene and intra-vaginal DHEA

Osteoporosis

Standard-dose ET and HT prevent bone loss in postmenopausal women by inhibition of osteoclast-driven bone resorption, a reduced rate of bone remodeling and reduces osteoporotic fractures.

When to start HT?

Hormone therapy is started depending on menopausal status of the patient and symptoms.

Women in late menopausal transition or early postmenopause

Cyclic combined regimens – continuous administration of 17-beta estradiol is started depending upon underlying co-morbidities.

- Cyclic administration of oral micronized progesterone, if there is uterus, for 10 days.
- For women with moderate symptoms, start with either transdermal estradiol 0.025 mg

twice weekly or oral estradiol 0.5 mg daily.

- For those with more severe symptoms start with a higher estrogen dose: transdermal estradiol 0.05 mg twice weekly or oral estradiol 1 mg daily and then titrate.

Women more than 2 to 3 years postmenopausal

Continuous combined regimens

- Estrogen is used (oral 17-beta estradiol 1 mg, transdermal estradiol 0.05 mg),
- Recommended progestin doses would be MPA 2.5 mg/day
- Natural progesterone 100 mg/day

Follow up

Endometrial monitoring is recommended in women with vaginal bleeding

Routine mammograms and breast examination are recommended in women taking MHT, even when used for short-term. There is duration-dependent increase in the risk of breast cancer diagnosis with both unopposed estrogen and combined MHT (7).

Duration of use

If hot flashes are completely relieved and the patient is tolerating the MHT well, continue the same regimen for at least for 5 years if the patient is in 40s

The standard recommendation for duration of menopausal hormone therapy (MHT) use has been five years or less (and not beyond age 60 years)

Extended use of MHT

Use of menopausal hormone therapy (MHT) should be individualized. Extended use of MHT is advised if the benefits from symptoms relief outweigh the risks (1, 3, 6). For women who choose extended use of MHT (more than five years or beyond age 60 years), restart estrogen at the lowest dose possible and make plans for a future attempt to stop the estrogen.

How to Stop

Abrupt withdrawal of exogenous estrogen at any age may result in the return of symptoms Women who taper MHT have lower

menopausal scores after stopping than women who stopped abruptly

Special populations

Primary Ovarian Insufficiency (POI)

POI is defined as menopause occurs before 40years. POI is associated with an increased incidence of cardiovascular, cerebrovascular disease and osteoporosis (8).

Hormone therapy is started at a younger age in these women, and all guidelines suggest that therapy should be continued until the average age of menopause to prevent premature bone loss, coronary heart disease (CHD), stroke, and an increased risk of dementia (1), (8).

Breast cancer patients

Though women with breast cancer often experience early menopause due to adjuvant chemotherapy and may have vasomotor symptoms due to Tamoxifen therapy, MHT should not be prescribed

History of ovarian or endometrial cancer

Women with low-risk disease, with menopausal symptoms, and in younger women MHT will decrease the long-term health consequences of estrogen deficiency.

Surgical menopause

In women who have undergone a hysterectomy and who are candidates for MHT, unopposed estrogen is given. Surgical menopause results in severe hot flashes. These women typically need a higher dose of estrogen in the first two to three years after surgery (e.g. 2 mg oral estradiol or 0.1 mg transdermal estradiol

Women with migraines

Migraine headaches are not considered to be a contraindication to MHT. For women with hot flashes and estrogen-associated migraines which typically worsen during perimenopause, Estrogen therapy often improves both symptoms.

Conclusion

The concept of 'lowest dose for the shortest period of time' may be inadequate or even harmful for some women. A more fitting concept is 'appropriate dose, duration, regimen, and route of administration' as said by the North American Menopause Society (3).

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Mind-Full MENOPAUSE

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"Ageing happens, but good health is planned"

The above saying could not be truer for a woman passing through menopausal transition. Each woman's experience of menopausal transition is unique, producing barely a ripple for some, it may summon waves in others, but for a few it is like an approaching storm (1). More than one-third of a woman's life is spent through menopausal years and hence it is imperative for clinicians to address her fears and concerns with compassion. Despite all the physiological changes, menopause should not be viewed as a sign of impending decline, but rather as a wonderful beginning of a good health program with lifestyle therapy as its cornerstone (2). Menopause needs to be redefined with emphasis on mind and body interventions enabling every woman to experience Mind-Full Menopause.

Lifestyle therapy with behavioral changes should be the first course of therapy and preventive healthcare in menopause. The four prongs of lifestyle therapy being nutrition and dietary pattern, physical activity and exercise, sleep hygiene and stress management and relaxation techniques (3).

Dietary prescription in menopause

"Let thy food be thy Medicine Hippocrates"

Healthy Menopausal diet should comprise of

- 50-60% complex carbohydrates with low glycemic index values and high fibre content
- 30% fat with less than 10% saturated fats
- 15% proteins

Primary source of complex carbohydrates should be whole grain cereals - unpolished rice, whole wheat, oats, millets, whole grain pulses, sprouts and soybeans. Total dietary fibre in daily diet should be 25 to 40 g/day (4). One can have about 100g fruit and 300g vegetables per day. Limit the use of cooking oil to two level tablespoon per day per person. Use mixed proteins with an average intake of 1g/kg/day. Include foods rich in phytoestrogens like lentils, kidney beans, soybean, dates, cherries and yam. Snack on 2 to 4 nuts a day like almonds or walnuts and few seeds a day like that of pumpkin or sunflower(4). Drink at-least 8 glasses of water a day. Drink 500 ml of milk or curd for adequate calcium reserve. Add up Vit C and Vit E rich foods such as wheat germ oil, green leafy vegetables, dried beans and nuts. Vitamin E is called the "Menopausal Vitamin" as it may have chemical activation similar to estrogen and it is also a powerful antioxidant. Vitamin C is important for collagen regeneration (3).

The right food in the right balance is the key to a balanced nutrition in menopause.

Keep mind over matter in food

Use the 4-step strategy of 'Stop'; 'Breathe'; 'Reflect';'Choose'; when eating food (1). Savour the food, appreciate the flavours and experience the enjoyment of eating-making each meal Mind-Full during menopause.

Physical activity and exercise

We do not dance to reach a certain point on the floor, but simply to dance "Alan Watts

Exercise should be a way of life in menopause and the focus should be on the experience rather than the goals. It has a larger picture during menopause than just weight control, as it improves sleep, boosts mood, sharpens mental function and improves sex life. The goals of exercise are health promotion, disease prevention and disability postponement (3). A well-balanced exercise program, comprising of aerobics, endurance, resistance, flexibility, posture and balance, as per health status of the woman, in relation to tolerability will benefit menopause (3). Exercise prescription should include

Aerobics

Resistance training

Stretching

The prescribed exercise should aim to burn 1000 to 1400 calories a week.

Aerobics

It can be done for 5-7 days a week for around 30 minutes (20-60 minutes)

Walking, stationary bicycling, swimming, cycling, aerobics dance with intensity based on the women's comfort, should be part of the aerobics schedule.

Resistance training

It can be done two to three times a week for 15-30 minutes.

Progressive resistance training exercises, using free weights or machines are important for muscle toning and muscle strengthening. It should be individualized and done under supervision till the woman masters it. It should provide stimulus for all muscle groups. 1 to 2 sets of 8 to 12 repetitive sets for 15 to 30 minutes should be the goal.

Stretching exercises

Stretching exercises are aimed at improving and maintaining flexibility. It should be done under supervision after each aerobics or resistance session (3).

To simplify it all, 30 minutes of some form of physical activity on most days of the week

should be on the "prescription"of menopause. It is never too late to start exercising (2). Being consistent is the biggest challenge and it can be overcome by making time, setting reasonable goals and finding joy in the process, and thus once again focusing on Mind-full exercise schedule.

Sleep

"When I wake up, I am reborn" Mahatma Gandhi

7 to 8 hours of sound sleep should form an integral part of menopause as it maintains energy, elevates mood,repairs and heal the body and helps to handle stress (3).

Stress management and relaxation techniques

"Mindfulness is both a meditation and a philosophy" Tibetan Buddhist principle

Each woman is unique, and she can select her own relaxation response techniques and make self-care and nurture, a priority in life. Self-care is not a luxury but a necessity. The different relaxation responses include breathing techniques, meditation, yoga, spirituality and repetitive prayer and mindfulness (1). Choose a time for relaxation, find a peaceful place, get comfortable, practice regularly and finally let go to lead a zestful life in menopause.

The mind is a powerful tool and it must be used wisely in menopause (1). A good healthy social network to communicate and a good sense of humor will help us to cope with the unexpected and smile through the unbearable moments. Thus, they are important ingredients for a Mind-Full Menopause.

Good health, a loving relationship, an understanding partner and positive attitudes are more crucial to sexual satisfaction in midlife. It is also important to exercise the brain by learning something new every day and keeping the brain busy to overcome the "brain fog" and memory loss that may hit one badly during the menopausal years (1).

Some of the most powerful women in the world gained their crowning achievement after the age of fifty. By nourishing the mind with positive thoughts and beliefs and tending to the body as a temple fortifying it with daily exercise, healthy nutrition, adequate sleep and mindful relaxation techniques, women can walk through menopause feeling invigorated, more confident, empowered and full of life.

"You don't stop having fun when you get old, you get old when you stop having fun"

With mind and body interventions women in menopause can truly look forward to a fun-filled Mind-Full Menopause and draw great arts of fulfilled lives on their life's canvas.

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A BOOST FOR THE BONES

Dr. Lalithambica Karunakaran
Former Professor and Head of the department of OBG, GMC Alappuzha, President, Alappuzha OBG Society

Life expectancy of women is increasing (1). Maintaining health of post-menopausal women is very significant as many women live one-third of their life after menopause. Osteoporosis and fractures in postmenopausal women cause significant morbidity and mortality. WHO defines osteoporosis as "a systemic skeletal disease characterized by low bone mass, measured as bone mineral density (BMD) and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fractures involving wrist, spine, hip, pelvis, ribs or humerus"(2). It is four times more in women than men.

Bone is a metabolically active organ with a continuous process of bone remodeling, balanced by osteoclastic and osteoblastic activity, influenced by cytokines, sex hormones, etc. Peak bone mass is attained by 25 -30 years.After the age of 35, osteoclastic resorption, increases over osteoblastic activity. With ageing and decline in estrogen level in menopause, there is net bone loss.

Factors predisposing to low bone mass (3):

1. Less physical activity in adolescence and young adulthood
2. Smoking

3. Less dietary intake of calcium and vitamin D
4. Increased life expectancy
5. Sedentary life, previous fractures
6. Excess caffeine, alcohol intake
7. Genetic factors like history of parental hip fractures
8. Prolonged use of drugs like heparin, Anticonvulsants, SSRI, corticosteroids, thyroxin, PPI like omeprazole, aromatase inhibitors like Letrozole

Types of osteoporosis:

Primary

Type I – Postmenopausal Osteoporosis: In early part of menopausal transition, affects trabecular bone.

Type II or senile osteoporosis: Age related, affects cortical and trabecular bone.

Secondary osteoporosis is due to underlying diseases like hyperparathyroidism, renal failure

Screening and Diagnosis:

- Dual Energy X-ray Absorptiometry (DXA) is the gold standard technology for bone density measurement. (3)
- Femur neck, hip and spine are usually measured.
- DXA result expressed as T score and Z score.
- T score– standard deviation between patient and average peak young adult bone mass.
  T-score < -2.5 is considered as osteoporosis.
  T-score between -1 and -2.5 is osteopenia.
- Z score- Standard deviation between patient and average bone mass for same sex age and ethnicity. This is used for premenopausal women; Score -2 reflect low bone mass
- Measurement of bone density at radius or calcaneoususing single X Ray absorptiometry–a cheaper method.
- Ultrasonography of calcaneus.

Primary prevention: Balanced nutrition, lifestyle modification, adequate Vitamin D and calcium intake, physical activity with weight-bearing exercise, avoiding bone depleting drugs. Peak bone mass is influenced by heredity and endocrine factors among which estrogen is the most important. There exists only a relatively narrow window of opportunity for maximizing bone mass. Almost all of the bone mass in hip and vertebral bodies in young women is procured in years, immediately following menarche and late adolescence. So supplementary calcium to children and adolescence is helpful to maximize peak bone mass in young women.

Early diagnosis:

1. **Risk assessment for fractures (4,5)**
   History: enquire about factors predisposing to osteoporosis and fractures
   WHO FRAX (Fracture Risk assessment Tool –country specific): can identify osteopenia group.
   Physical examination: record height and weight annually, check for balance and gait
2. **DXA:** of spine and hip in all women > 5 years after menopause and less than 5 years in women with two risk factors is recommended.
3. **Laboratory tests to rule out secondary causes:** S.PTH, Ca, Phosphorous and Alkaline-phosphatase for primary hyperparathyroidism, RFT–for secondary hyperparathyroidism, from renal failure.

Treatment option for fracture risk reduction

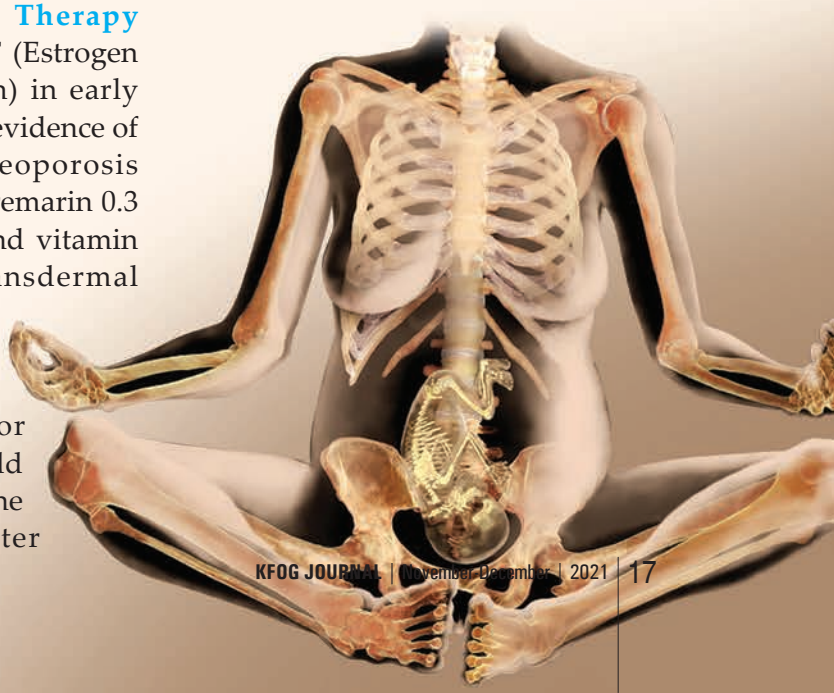
1. Therapeutic life style modification: Balanced diet with adequate protein (0.8 -1g /kg), exposure to sunlight, optimal physical activity (4), avoiding bone depleting agents like caffeine (< 3 cup/ day), alcohol, tobacco, and excessive salt. (5g/day)
2. Calcium intake 800-1000 mg /day
3. Vitamin D: sunlight exposure to 15-30% body surface area, Vit D supplement (2000IU/day)

4.Pharmacotherapy(3,4,5): Indications

i. Fragility fractures (clinical, height loss > 4cm, kyphosis)
ii. BMD T score < -2.5
iii. Women with LBM and risk factors
iv. If BMD measurement not possible, use fracture risk tools like FRAX, OSTA (Osteoporosis Self assessment Tool for Asians) or SCORE (Simple Calculated Risk Estimation Score)

The choice of drug is based on factors like age, years since menopause, comorbidities, cost factor and balancing risk and benefit of each medication.

1. **Menopausal Hormone Therapy (MHT):** Initiation of MHT (Estrogen or Estrogen andProgestin) in early menopausal women with evidence of low bone mass and osteoporosis reduces risk of fracture. Premarin 0.3 mg along with calcium and vitamin D is a good option. Transdermal estradiol 0.5 /1 mg/day also can be given. MHT can be continued for 10 years after evaluating for contra-indications.It should not be started solely for bone protection, 10 years after menopause. The benefit on bone density is lost after stopping MHT. MHT is indicated in POI as primary therapy for preventing bone loss. Progestin should be added to estrogen in women with uterus.
2. **Tibolone:** in women with mammographic density instead of MHT, also along with GnRH analogue to preserve bone density. Not to be used in women above 60 years, breast cancer treated, with risk factors for stroke
3. **SERM: Raloxifene:** produces favorable estrogen like response in bone and lipids, with no endometrial proliferation, has antiestrogenic effect on breast. Dose is 60 mg/ day, reduce fracture risk, especially useful in women with increased breast cancer risk, risk of VTE same as that of estrogen, found to be low in healthy postmenopausal Asian women. Adverse effect on hot flushes.
4. **Bazedoxifene:** 3rd generation SERM, favorable effect on bone and lipids. Does not affect breast and endometrium. Dose 20 mg/day. No adverse



effect on hot flushes.

5. **Combination of Bazedoxifene 20 mg and Conjugated Equine Estrogen 0.3 mg** is a promising option for reducing risk of osteoporosis. FDA approved for treating osteoporosis, vasomotor symptoms and genito-urinary symptoms.
6. **Teriparatide: Recombinant Parathormone:** Reserved only for women with high risk of fracture like very low BMD, and previous vertebral fracture. Dose 20mcg/d daily s/c for 18 months. High cost is a drawback. Prolonged therapy not advised because of risk of osteosarcoma.
6. **Bisphosphonates:** anti resorptive therapy. Alendronate or Risedronate are commonly used, can be given as first-line therapy or after discontinuing teriparatide
7. **Calcitonin:** Approved for treatment of postmenopausal osteoporosis, not for prevention. Helps to relieve pain for vertebral fractures, for short period only.
8. **Denosumab:** Human monoclonal antibody. It blocks osteoclast maturation, function and survival reducing bone resorption. It increases trabecular and cortical bone strength, reduces fracture risk, increase BMD more than bisphosphonates. Provides benefits over 10 years without drug holiday. 60 mg S/C every 6 months, patient convenience, well tolerated even if creatinine clearance <30ml/mt, where bisphosphonates and tereparatide are contraindicated. Unlike alendronate antiresorptive action persists for some time after cessation of treatment.But follow up is recommended

Guidelines for monitoring response to therapy

Follow-up by BMD (DXA) testing. there is no consensus on the optimal frequency of monitoring and preferred site to monitor. Biochemical markers of bone turnover also may be used. There are no prospective trials to define the most optimal approach for incorporating markers into monitoring strategies

Conclusion: WHO has identified osteoporosis as an important non communicable disease. Maintaining bone health of post-menopausal women is very significant. Gynecologist has an important role in creating awareness to ensure prevention, proper screening and treatment.

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MENOPAUSE
A MAN'S PERSPECTIVE

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Menopause is a normal, natural event defined as the cessation of menstruation and is confirmed when menstrual cycles cease to occur for a period of one year. It is one of the milestones in a woman's life. It generally occurs between the age of 45 and 55 years.

Since menopause is synonymous with womanhood, I wondered what it had got to do with men. Well, then I realised, men may not have any role in the physiological process of

menopause. But they certainly have a lot to offer to the woman, who is navigating the troubled waters of that unique experience.

Menopause presents with many major and minor symptoms. The major ones are vasomotor (hot flushes and night sweats), sleep disturbances (Insomnia), vulvovaginal-symptoms (Dyspareunia and reduced libido) and psychological symptoms (depression, anxiety and mood swings). All these can be quite disturbing to the woman and can affect her quality of life.

A typical picture of a woman in menopause is a fifty-year-old lady, who has just seen her children leave home for work or higher studies. She may be in a senior position in her professional life with lots of added responsibility or a person with financial difficulties. She will be having her husband/ partner by her side or may have just become a divorcee or widow recently. Or worse, she may just be recovering from a major surgery (hysterectomy with oophorectomy) which must have abruptly consigned her to a surgical menopause.

Some of the husbands/ partners may also be in the male equivalent of menopause, called 'Andropause'. Andropause is a much more insidious and gradual process compared to menopause and the symptoms are nowhere as similar. But the presence of Andropause means the males will have their own battles to fight. Even then, it is worth giving a hand to the lady of the house in her time of need.

We will start with the most common symptoms – hot flushes and night sweats. This makes the lady very irritable. This automatically results in mood swings the effects of which extends to her family and work. Night sweats will affect sleep and the reduced hours of sleep and rest will contribute to the problem.

How to improve things at home?

At home, the males of the household – husbands/ partners, sons – should be understanding of the whole situation. It will be good if the lady's workload can be reduced. A helping hand in the kitchen by the menfolk will go a long way in cooling the lady down (literally and figuratively). Make sure she takes her medications but do not be insistent about it. Men should take care of their own attire and chores rather than leave it to the lady. Any activity which raises stress levels should be toned down. Remember that she has been having your back, your entire life. A little support now will be worth a lot.

How to improve things at work?

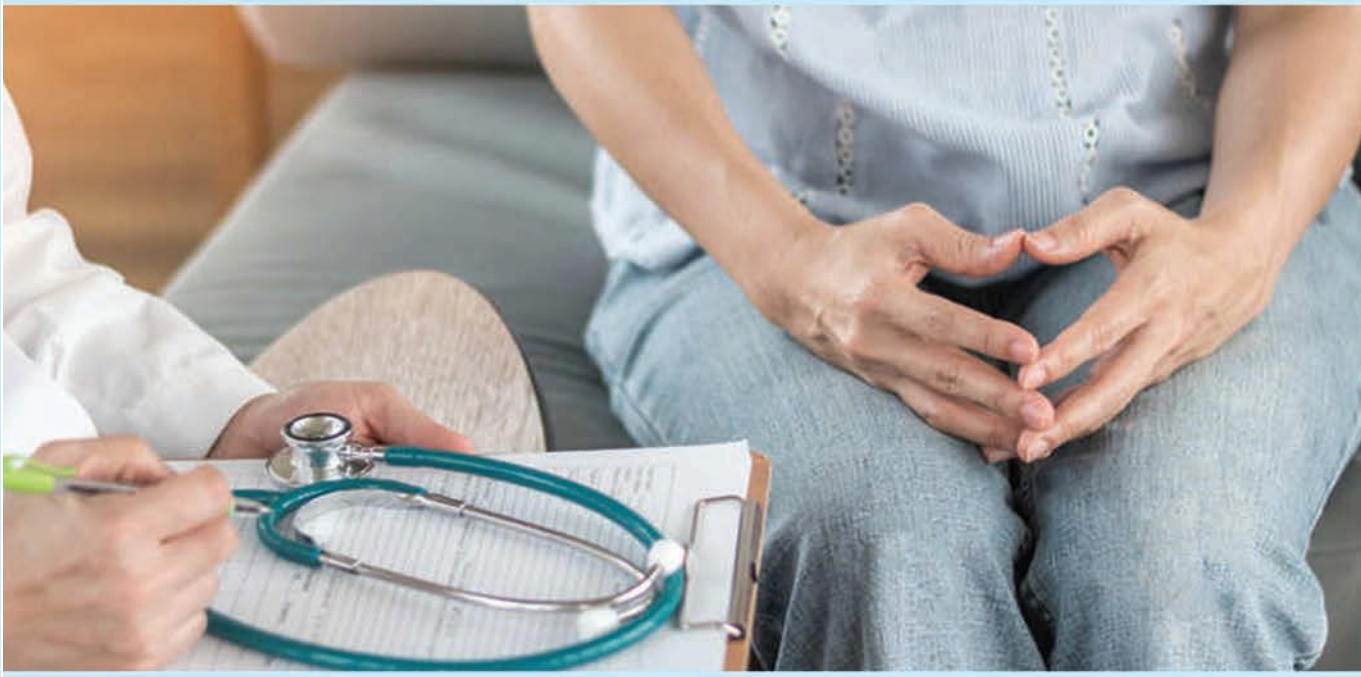
The irritability and mood swings will mean that her co-workers will not be having it easy. They will be at risk of being at the wrong end of a sharp tongue, even for minor matters. This is true for both male and female colleagues. It is not an ideal scenario but small gestures do make a difference. If the boss is a male, he can try to put in a quiet word to the lady about the effect she is having on others. If you are a junior, do the work efficiently and within the allotted deadline to avoid flare ups. Confronting the lady or an aggressive mentality towards her will only worsen matters. If nothing works, simply stay out of her way.

Menopause can also occur

following surgery (Hysterectomy with oophorectomy). Here, the onset of symptoms is abrupt and this can be quite upsetting to the lady. During natural menopause, at least the woman is prepared for what is coming whereas in surgical menopause, everything happens fast. The male partner should give adequate moral support at this juncture which will help the lady tide over the initial rough days. Sometimes, all he needs to provide, is a shoulder to cry on. The feeling of having lost her ovaries may add an extra dimension to her feelings and aggravate her emotions. Some tender loving care from the male partner can work wonders.

One of the more disconcerting symptoms of menopause is the vulvovaginal atrophy due to lack of Oestrogen. This combined with reduced libido results in the sexual life of the couple going for a toss. Sexual activity can be painful to the lady but lack of it can also be difficult. The male partner has to be very understanding in this situation. The choice regarding sexual activity should be left with the lady. The main symptoms of menopause generally subside in a few years and things can often return to normal after that. This fact should be remembered by the couple and it can help them tide over some rough days.

To summarize, menopause is a milestone in a woman's life, on the scale of menarche and childbirth. The fact that it comes later in her life may make it difficult for the woman to adjust and get by. A helping hand from the husband/ partner/ family can go a long way. Once the major symptoms of menopause subside, the quality of life generally returns to the previous times. As such, support by the menfolk during the tough times of menopause immeasurably improves the lady's well-being.



CUSP OF THE CRAB IN MENOPAUSE

The average life expectancy of menopausal women has increased. This brings with it, issues related to cancer disease, prevention and management. The burden of gynaecologic cancer is rapidly increasing world over. The article touches on the two major gynecologic cancers, **Endometrial cancer (EC) & Epithelial Ovarian cancer (EOC)**[1,2]

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Endometrial cancer (EC)

Thee are two types of EC

Type I	Type II
More Common (85%)	Less common
Younger women	Older women
Precursor lesion of atypical hyperplasia seen	Non endometrial histology (serous, clear cell, grade3 tumours)
Well-differentiated	Poorly differentiated
Associated with hyper-estrogenism	Atrophic endometrium, Aneuploid (K-ras, HER2/neu, P53 overexpression)
Minimal myometrial invasion	Can present in advanced stage
Favourable outcome	Poor outcome and increased relapses

Risk factors

a. Age is the most important risk factor. The median age at diagnosis of 60 years. About 85% of cases occur after the age of 50 years. Most cases of endometrial carcinoma are sporadic.

b. Use of unopposed estrogens as part of hormone replacement strategies. A meta-analysis of 30 studies showed that the relative risk of ever-users of estrogen therapy was 2.3 compared to non-users, and it increased to 9.5 in users of 10 or more years.

c. Obesity

d. Diabetes
Hyperinsulinemia and increased levels of insulin-like growth factor 1 are believed to have neoplastic potential.

e. Tamoxifen: It is a SERM with antiestrogenic properties in the breast but estrogenic effects in the uterus. The findings of the NSABP B-14 trial show a relative risk of 7.5 of EC in tamoxifen users with greatest cumulative risk after 5 years of tamoxifen use. Aromatase inhibitors prevent estrogen synthesis and hence third-generation aromatase inhibitors (anastrozole, letrozole, exemestane) are replacing tamoxifen in breast cancer patients [3].

Protective factors and prevention

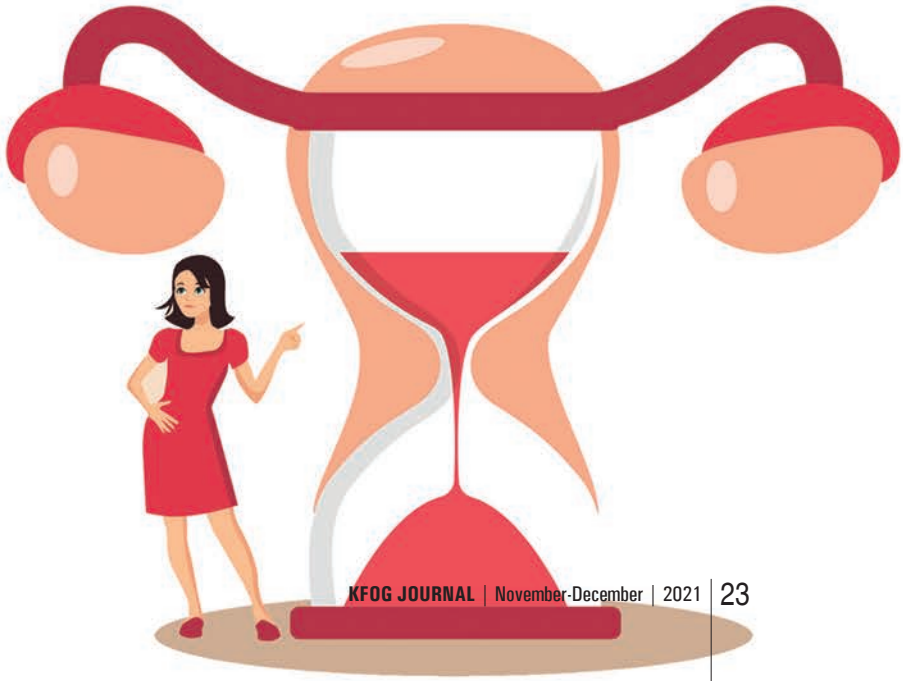
Weight loss and exercise
Adding progestins to estrogen in women with an intact uterus
Patients with hyperplasia with atypia should be offered hysterectomy. A GOG trial has shown that 40% of patients with a preoperative diagnosis of atypical hyperplasia had uterine carcinoma.

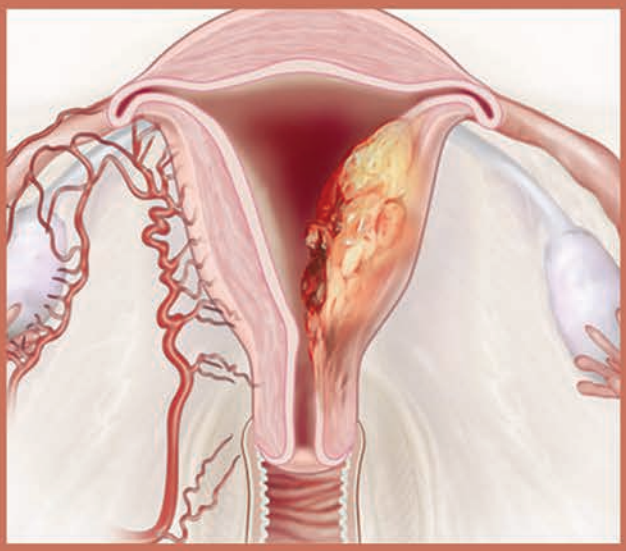
Screening

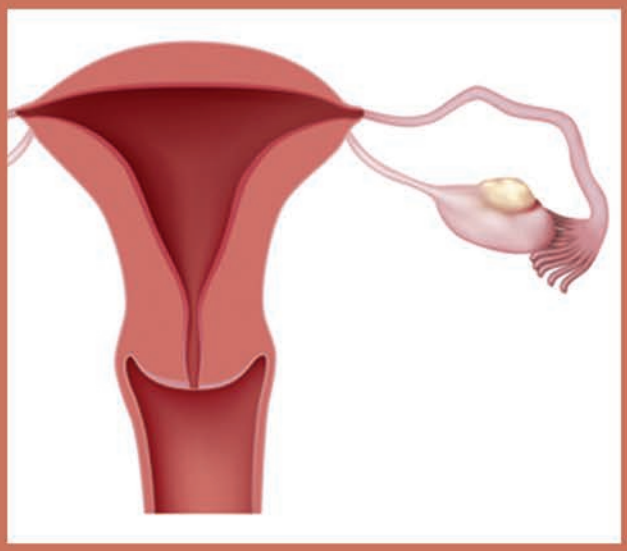
The ACOG and the Society of Gynecologic Oncology do not recommend routine screening of patients for uterine cancer. The American Cancer Society does recommend annual endometrial biopsies starting at age 35 for women known to have or to be at risk for HNPCC.
It is mandatory to evaluate any women with postmenopausal bleeding or spotting.

Clinical presentation

Classic symptom of endometrial carcinoma is abnormal uterine bleeding. Around 10% of patients with post-menopausal bleeding are found to have EC on biopsy. Patients may present with vaginal discharge, or have an incidental sonological finding of thickened endometrium, or may show abnormal cervical cytology. Patients with intraperitoneal disease may present with complaints like that of







patients with ovarian cancer. The measurement of endometrial thickness (ET) has been shown to best predict the absence of carcinoma, with a false-negative rate of 4%, using a threshold value of <5 mm

Management

Management of most patients with EC remains surgical and includes, an initial surgical exploration with collection of peritoneal fluid for cytologic evaluation, thorough inspection of the abdominal and pelvic cavities, with biopsy or excision of any extrauterine lesions suspicious for tumour, and total extrafascial hysterectomy with BSO and bilateral pelvic and para-aortic lymph node dissection. Minimally invasive surgery must be done when feasible. Based on risk assessment radiation and chemotherapy may be added as required

Epithelial Ovarian Cancer

"The silent killer" or "the cancer that whispers!!" Because usually by the time it is diagnosed, the cancer is at an advanced stage. EOC is the leading cause of death from gynecologic cancer. The fatality rate of ovarian cancer is high (70%), and 80% of deaths occur within 5 years of diagnosis.

Risk factors

Having a first-degree relative with the disease
Age: Fifty percent of all cases of ovarian cancer occur inwomen over the age of 65.
Early menarche
Late menopause
Use of both estrogen only and estrogen–progesterone HRT (However Low dose HRT can be prescribed to patients with severe postmenopausal symptoms and current recommendation is to administer it at the lowest effective dose for less than 5 years)

Protective factors

Increased parity
Breast-feeding,
Use of OCP for at least 5 years
Tubal ligation

Clinical presentation

Most common symptoms of ovarian cancer are bloating, pelvic or abdominal pain/discomfort; vague but persistent gastrointestinal upsets such as gas, nausea or

indigestion; difficulty eating or feeling full quickly; urinary symptoms; unexplained changes in bowel habits; unexplained weight gain/loss; ongoing unusual fatigue; back pain; menstrual changes; pain during intimacy.

Ultrasonogram

On average, the volume of a normal ovary is 10 cm^3 in postmenopausal and 20 cm^3 in premenopausal women

In postmenopausal women, asymptomatic, simple unilocular unilateral cysts, less than 5 cm in diameter with normal CA-125 can be managed conservatively with follow-up 4-6 monthly. In postmenopausal patients with complex adnexal mass and in those with solid masses should be offered surgery

Tumour Markers

The CA-125 marker (normal <35 U/mL), is the most common one used. 80% of patients with ovarian cancer of any stage who are over 50 years have an elevated CA-125.

The Risk of Malignancy Index (RMI) can triage women with ovarian cysts into low or high risk of malignancy. RMI score of 200 (sensitivity 78%, specificity 87%) can predict the likelihood of ovarian cancer [4]

Human epididymis (HE)4 is a secreted glycoprotein expressed on human ovarian cancer cells with a sensitivity of 74% and specificity of 87% in the differentiation of benign and malignant adnexal masses.

Treatment

Treatment of EOC is surgery- staging surgery in early-stage disease, while a surgical debulking to no residual disease is offered in late stage disease. Patients with ovarian cancer will benefit from treatment by a gynecologic oncologist. Optimal staging in early ovarian cancer includes careful inspection, palpation, and biopsies of peritoneal surfaces (diaphragm, paracolic gutters, bladder, and cul-de-sac peritoneum), pelvic and diaphragmatic washings, removal of the affected ovary, an infra-colic or infra-gastric omentectomy, and a systematic pelvic and para-aortic lymph node dissection. Every effort should be made to remove an ovarian mass intact. Surgical debulking is central to the initial management of advanced FIGO stage III/IV ovarian cancer, and the extent of residual disease after surgery is the only prognostic factor under the control of the operating surgeon. Chemotherapy, either adjuvant or neoadjuvant, may be used based on performance status of the patient, disease load and resectability.

Hence a careful evaluation of these cases by the clinician is of utmost importance and clinical judgement and decision making must be based on sound knowledge enabling for an expert management of these cases.

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FERTILITY IN MENOPAUSE: PROBLEMS AND SOLUTIONS

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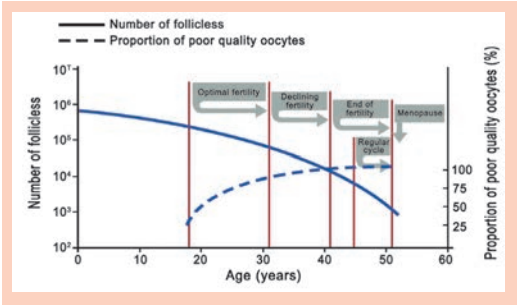
The menopause is a certainty for all women and is unavoidable. Menopause is the permanent cessation of menses due to loss of ovarian follicular activity. It is defined retrospectively after menses has stopped for 12 months in a previously menstruating patient.(1) Perimenopause is the interval preceding menopause characterized by irregular menstrual cycles with associated endocrinologic changes and symptoms of hypoestrogenism. Average duration is 4 years. Primary ovarian insufficiency (premature ovarian failure) is loss of ovarian function before the age of 40 years. It is not definitively known if amenorrhea represents menopause, therefore, in most patients, the distinction between primary ovarian insufficiency and premature/early menopause is made in

retrospect. Usually, it is treated as synonymous with premature or early menopause, although there is still potential for menses to resume and pregnancy to occur. The menopause marks the loss of fertility caused by the depletion of ovarian follicles, an event that is also brought about oophorectomy or by radiotherapy or chemotherapy which damages the sensitive ovarian tissue. A million or so germ cells are present at birth of which majority undergoes atresia. Ovulation during the reproductive life span would only account for approximately 400 oocytes. This atresia accelerates from the age of 37 (2). With the loss of oocytes, the primordial follicles that enclose them do not respond to pituitary gonadotropin stimulation and the major source of estrogen is lost.

Human menopause with fertility ending before life is an enigma from an evolutionary viewpoint. True menopause is extremely rare in the animal kingdom, and virtually unique to humans. Evolutionary explanations for menopause suggest that the climacterium is evolved to prevent mothers from reproducing late in life, when the benefits of reproducing may be small, hence with intense reproductive investment early in life. In humans, offspring are born helpless and have a long period of dependence. And benefits of reproducing late may also be small because pregnancies in old age have an elevated risk of miscarriage, the fetus of old mothers has a higher risk of being born dead, having a defect or being born small. In addition, late reproduction may be costly, for a mother that dies during or shortly after childbirth will not only jeopardize the life of her current child, but also those of earlier children which are still dependent on their mother for sustenance and protection.



Classification

The 2011 ***STRAW + 10***, Stages of Reproductive Aging Workshop (STRAW) criteria (3), reviewed advances in under standing of the critical changes in hypothalamic-pituitary-ovarian function that occur before and after the final menstrual period.

Workshop(STRAW) + 10 staging system

Menarche — FMP(O)

Stage	-5	-4	-3b	-3a	-2	-1	+1a	+1b	+1c	+2
Terminology	Reproductive				Menopausal Transition		Postmenopause			
	Early	Peak	Late		Early	Late	Early			Late
					Perimenopause					
Duration	Variable				Variable	1-3years	2 years (1+1)		3-6 years	Remaining lifespan
PRINCIPAL CRITERIA										
Menstrual Cycle	Variable	Regular	Regular	Subtle changes in Flow/ Length	Variable Length Persistent ≥ 7-day difference in length of consecutive cycles	Interval of Amenorrhea of >=60 days				
SUPPORTIVE CRITERIA										
Endocrine FSH AMH Inhibin B			Low Low	Variable* Low Low	↑Variable* Low Low	↑>25 IU/L** Low Low	↑Variable* Low Low		Stabilizes Low Low	
			Low	Low	Low	Low	Very Low		Very Low	
DESCRIPTIVE CHARACTERISTICS										
Symptoms						Vasomotor symptoms Likely	Vasomotor symptoms Most Likely			Increasing symptoms of urogenital atrophy

*Blood draw on cycle days 2-5 ↑= elevated
*Approximate expected level based on assays using current international pituitary standard [97-69]

Thus, the lady who comes with fertility issues can be in the late reproductive stage (*stage -3b, stage -3a*), early menopausal transition (*stage -2*), late menopausal transition (*stage -1*), menopause, early post-menopause (*stages +1a, +1b, +1c*) and late post menopause (*stage +2*).

When a patient with menopausal symptoms presents, always rule out

a) Pregnancy, by measuring ß-hCG in amenorrheic patients of reproductive age who are not using a reliable form of contraception.
b) Thyrotoxicosis, distinguish from menopausal transition or menopause with thyroid function tests. TSH level falls below the lower limit of reference range in hyperthyroid states but within reference range in perimenopausal and postmenopausal patients
c) Hyperprolactinemia, differentiate with prolactin level, which is within reference range in perimenopausal and postmenopausal patients. Occurs in several pathologic pituitary conditions or can be induced by drugs in several classes, including antipsychotics, antidepressants, and H2 receptor antagonists. Presenting symptoms can include galactorrhea or headache; the latter is observed in the presence of a mass caused by a pituitary adenoma.
d) Primary ovarian insufficiency (premature ovarian failure, premature menopause) Elevated levels of follicle-stimulating hormone (FSH greater than 20 units/L) with low estradiol levels (E2 less than 30 pg/mL) on 2 occasions (at least 4 to 6 weeks apart) are consistent with a diagnosis of primary ovarian insufficiency.

Treatment of Age-related Infertility

Women may be offered COH with clomiphene citrate or gonadotropins or IVF to improve their chances of pregnancy and decrease time to pregnancy in age related infertility. In one retrospective review of more than 4000 treatment cycles using clomiphene citrate and IUI, pregnancy rates were 7% for women aged 38 to 40, 4% for women 41

to 42, and 1% for women >42 (4). Older women may consider 1 to 2 cycles of COH if they do not want to try IVF as a first-line treatment, but they should move on to IVF quickly if they are unsuccessful within the first couple of cycles. Even with IVF success is limited. A study found a significant drop in IVF live birth rates in women >43 years (5). Live birth rates were 7.4% for women aged 40 to 42 and only 1.1% for women >43 years. Also, miscarriage rates were 43.1% in the younger age group and 65.2% in the older age group (5).

A woman with decreased ovarian reserve should be offered oocyte donation as an option because pregnancy rates associated with this treatment are significantly higher than those associated with controlled ovarian hyperstimulation or in vitro fertilization with a woman's own eggs (2). Pregnancy rates with oocyte donation are based on the age of the donor, not the recipient. Pregnancies and live births have been reported in women into their 60s; however, the use of donor eggs for women after age 50 is controversial.

Pregnancy in women >40 years, is also associated with a higher risk of obstetrical complications, including surgical delivery, gestational diabetes, preeclampsia, intrauterine growth restriction, and low birth weight. Pre-conception screening for significant medical conditions such as hypertension or diabetes should be considered for women at high risk before fertility treatment is begun.

Fertility Preservation and Restoration Options for Young Female Cancer Patients

When the estimated risk of gonadotoxicity from cancer therapy is greater than 50%, fertility preservation strategies should be offered to young patients (<40 years of age) prior to starting treatment. Established options include embryo freezing and egg freezing. Debatable options include ovarian protection techniques such as treatment with GnRH analogues and hormonal suppression, surgical ovarian transposition (oophoropexy), gonadal shielding, and the use of fractionated chemotherapy and radiotherapy. Experimental options include ovarian tissue freezing for use in future auto-transplantation, oocyte in vitro maturation (IVM), artificial ovary systems, stem cell transplantations, and neoadjuvant cytoprotective pharmacotherapy

Conclusion

Better understanding of the genes and enviomental factors that impact ovarian reserve may provide greater insight on the process of reproductive aging and the genetic requirements of human fertility. While developments in the treatment of infertility are to be welcomed, there are financial, social and ethical implications in procedures involving the use of fetal material and also in offering motherhood to those who have reached the menopause.

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