MODULE  4

Case Studies
Case Studies—Interaction
Management Plan At Menopause

Group 1 (GP 1) - Women Without Menopausal Symptoms

Group 2 - (GP 2) Women With Menopausal Symptoms
Case -1

- 48 yr old, asymptomatic
- Getting regular periods heard she will have lot of problems at menopause
- Wants to know what medication to take to avoid problems of menopause
- Contraception-Vasectomy  physical examination and investigations normal
- How will you counsel her?

GP1 WITHOUT DISEASE
Average age at menopause in India in yrs—48/46/52?

Why is it important to know?
What stage of reproductive aging is she in?
• FSH is needed to diagnose menopause, especially if the woman is worried about the change ——Yes/No

• How will you counsel her?

• Natural phenomenon, many have no problems

• Some women may develop symptoms
Wants to Know What Medication to Take to Avoid Problems of Menopause
Case -2

- 44 yr old, P1 A1
- C/o Irregular periods since 6 months, 3-4/25 -40 days
- LMP: 2 months ago
- Using condoms
- No visits to Gyneac since delivery
- BMI: 26, BP: 120/80
- TSH 2 mIU/L; FSH 8 mIU/mL

GP 1 WITHOUT DISEASE
Concerns

• Is this menopause?

• Can I get pregnant?

• Are the irregular cycles normal?
Is irregular menstrual cycle a symptom of menopause?

Yes/No
Case -3

- Mrs. R.  
  Age 48Yrs.
- Reached menopause 2 years ago
- Asymptomatic/Symptomatic
- Occupation - Beautician

Concern :-

- Growing more coarse hair on the upper lip and chin since
- The time of cessation of her periods
- Gaining more weight especially around the waist & hips

GP 1 /2 WITHOUT DISEASE
Weight

• The body expands to accommodate all the love and wisdom that comes with aging

• Only proven solution—Diet and Exercise

• At menopause transition there is a redistribution of weight from a gynecoid to an android form.

• No increase in weight with HT -unless Progestogen sensitive
What advice can we give our patients?

- Lifestyle, diet, exercise, Ca and Vit D

- Supplements, Screening tests—-
  
  GROUP 1
  GROUP 2
  MHT-CONTINUOUS SEQUENTIAL
Case -4

- 50 yr, Para 1 presents with c/o recurrent urinary infections
- Amenorrhoea since 10 months
- Cycles 2-3/60-90 days since preceding year
- H/O having gained 5 Kgs in the last 6 months
- c/o lethargy and fatigue all the time

GP 2 WITH DISEASE
• Gen & Systemic Exam : NAD
• P/S : curdy white discharge
• P/V : NAD
• Provisional Diagnosis?
• Differential Diagnosis?
• Investigations?
Results

• Hb : 12 gm% WBC :7,000
• BSL(F) 165 mg%, (PP) 270 mg%
• Urine Routine : NAD
• TSH 16 ulU/ml
• FSH 48 IU/L
• USG: Uterus normal size, endometrium 4mm, ovaries 2.1x3x2 cm and 2x3x2.4 cm
Treatment?

• TLSM-Therapeutic Lifestyle Management

• Endocrine reference

• Treat Hypothyroidism, Diabetes Mellitus
Case -5

- 44 yr old woman for health check
- Asymptomatic/hot flushes
- Hypothyroid, on Thyroxine since 12yrs
- Sister had a Hip fracture at age 54
- BMI 18

**What is her main risk?**

**GP1/GP2 WITH DISEASE**
The result of DXA: T Score -2

Osteopenia
Interpretation of Results

• Osteopenia - 2 fold increase in fracture compared with normal

• Osteoporosis - 4 to 5 fold increased risk of fracture

• Severe osteoporosis - 20 fold increased risk of fracture
What Is The Treatment Of Choice?

As the patient has significant hot flushes and has no contraindication, HT may be the option of choice.
» If the woman is perimenopausal—your prescription options for MHT

» If the woman is one year postmenopause—your prescription options for MHT
Guideline

- HT appropriate first line therapy for women under age 60 with increased risk of fracture
- HT cessation, protective effect declines
- Not recommended after 60 for sole purpose of prevention of fractures
HT - Bone

Perception
• HT should not be used for bone protection because of its unfavorable safety profile
• HT could only be considered when other medications failed, were contraindicated or not tolerated, or in the very symptomatic woman
Evidence

• For the age group 50-59, HT is safe and cost-effective

• Overall, HT is effective in the prevention of all osteoporosis-related fractures, even in patients at low risk of fracture [A]
HT-Bone

Perception
HRT is not as effective in reducing fracture risk as other products (bisphosphonates, etc.)

Evidence
Although no head-to-head studies have compared HRT to bisphosphonates in terms of fracture reduction, there is no evidence to suggest that bisphosphonates or any other antiresorptive therapy are superior to HT
Case -6

- 50 yr old, High profile job
- Underwent TAH, BSO for Fibroids / endometriosis 2 months ago
- Presents with hot flushes since 1 month
- Gyneac said to have Soya & Tofu
- No relief, come for second opinion
- Clinically NAD

GP 2 without disease
• Should ovaries have been removed?
  • Why not?

Ovaries continue to produce androgen after menopause, which is useful for bone health, mood and libido

• What about the tubes?
Preferable to do salpingectomy to avoid hydrosalpinx and may be Ca Ovary

• Management?
After counseling, chose to have HT—Which one and what regime would you give
• Reports after 6 months

• Company doctor told her to stop HT

• Now has memory lapses & insomnia

• Ref to Psychiatrist

What would you do?
Surgical Menopause

- Routine HT is not recommended for surgical menopause in postmenopausal women as primary prevention for chronic conditions.
- HT should be considered in women less than 50 who have undergone surgical menopause.
HT and Endometriosis

• In women with surgically induced menopause or natural menopause because of endometriosis, estrogen/progestagen therapy or tibolone can be effective for the treatment of menopausal symptoms (Al Kadri, et al., 2009)

• Clinicians continue to treat women with a history of endometriosis after surgical menopause with combined estrogen/progestagen or tibolone, at least up to the age of natural menopause
Case -7

- 60 yr old
- H/o CABG for CAD 2 yrs ago
- C/o night sweats, nocturia, frequency, urgency, joint pains & backache
- Urine Routine : PC 15-20
- Culture : No growth
- BSL F :102 & PP: 136
- BMD : T Score at LS : - 1.8

GP2 with disease
• Was on HT before surgery
• Wants to go back on it

What would you do?

• TLSM
• Vaginal Estrogen Cream
• Bisphosphonates
• HT?
Evidence

- No role of HT for secondary prevention
- Secondary prevention of CVD should be by non-hormonal methods
Case -8

- 46 yr old, anxious woman
- Mother has Alzheimer’s
- Asymptomatic
- Clinically NAD
- Has heard that AD can be prevented by HT
- Asks for your opinion

GP1 without disease
Case -9

- Obese, 42 year old perimenopausal women who seek relief of menopausal symptoms, who also desire contraception, and who in some instances need control of bleeding when it is heavy

- With no Risk Factors

GP2 without disease

HOW DO WE MANAGE?
Case -10

• 51-year-old woman presented with frequent and distressing hot flushes that interfere with her work and sleep, and vaginal dryness that makes sexual intercourse with her husband uncomfortable

• She is otherwise healthy, menopause 10 months ago

GP2 without disease

HOW DO WE MANAGE?
Case -11

• 46-year-old healthy female, presents with a complaint of severe insomnia and mood changes in the last few months, increased emotional liability, and crying outbursts. Complaints - Palpitation, fatigue, giddiness, insomnia - since six months

• Experienced difficulties in falling asleep for many years, particularly in the week prior to her menses, when she usually feels ‘wired before going to bed’, ‘worried and irritable about everything’, ‘can’t turn it off’. During this time, it usually takes half an hour or longer to fall asleep. She also suffered from mood changes in the premenstrual period
Never sought treatment because “it was not severe enough to affect her job or concentration the next day”, and “it would go away when the periods come”

• Last menstrual period - 9 months ago

• Lab values: FSH = 36, Hb-9gms, Seen by Neurologist, Cardiologist, Gynecologist. Referred to a Psychiatrist

GP2 with disease

HOW DO WE MANAGE?
Differential Diagnosis

• Anaemia

• Anxiety Neurosis

• Perimenopausal syndrome
Treatment

• HT/ SSRI Fluoxetine 20mg/OD

• Haematinics

• Life style modification
Case -12

• 46 years old healthy women, P2, breast fed
• Severe hot flushes, night sweats, insomnia, mood changes, loss of libido since 18 months
• LMP - 10 months ago
• H/O premenstrual breast pain
• Breast cyst aspirated 3yrs ago
• Screening- Mammogram benign with dense breast
• After WHI previous reports refused Hormone Therapy, preferring Non hormonal therapy for the past six months
• Unhappy with the relief has come back for consultation

GP2 with disease
Would you offer HT?
Fears

• Close friend had a breast tumor

• She was afraid that her cyst would produce pain or neoplasm

• Although she didn’t want irregular bleeding she was willing to accept a regular predictable vaginal bleed
Motivation

• Flushes, night sweats, bad sleep, mood changes and libido loss

• Preserve good interpersonal relations

• Regain normal performance in work

• Increase bone mineral density
 Which is preferred option?

- Combined cyclic HT
- Continuous combined HT
- Oral contraceptive
- Tibolone
- Raloxifene
- Phytoestrogens
- Fluoxetine, Clonidine, Gabapentin
Breast

Perception

All types of HT cause an increased risk of breast cancer within a short duration of use

Evidence

In the WHI estrogen-only arm, there was no increase in breast cancer risk for up to 7 years. However, the risk of invasive breast cancer was significantly lower in first-time users of estrogen. [A]

In observational studies, a small increase in risk during estrogen-alone therapy was recorded only after long-term use. [B]
HT and Breast Cancer

- No clear evidence that HT causes breast cancer
- Overall risk of breast cancer while on HT is low
- Women who develop breast cancer while on Ht have better survival rates than those not on HT
- A family history of breast cancer does not further increase risk of breast cancer while on HT
Breast

Perception
All types of HRT cause an increased risk of breast cancer within a short duration of use

Evidence
After 5 years’ use of combined estrogen and progestogen, the WHI cohort showed a small increase in risk of breast cancer of about eight extra cases per 10,000 women per year. Risk was not increased in first-time hormone users [A]
Risk Factors For Breast Cancer?
Mammogram- Dense Breast
Non-modifiable risk factors for breast cancer are age, family history, benign breast disease, BRCA - Breast Cancer 1 or 2 carriers, early menarche (<12 years), late age at menopause (after age 55), increased breast density chest irradiation between ages 25 years and 55 years
Modifiable risk factors are age at first child, breast-feeding, parity, obesity, physical activity, alcohol, menopausal HT
Breast cancer screening includes 3 methods of early detection (Grade C)

- Breast self-examination (BSE) monthly starting in the 20 s

- Clinical breast exams (CBE) every 3 years starting in the 20 s till 39, and annually thereafter

- Mammographic screening (annually) starting at the age of 40 years
In India, breast cancer incidence peaks before the age of 50 years and a recent review of the evidence in younger women (aged 39–49 years) based on 8 trials conducted between 2001 and 2008 suggests that mammographic screening is also beneficial in this younger age group.

An approximate 12–15% reduction in breast cancer mortality is associated with mammography screening for women aged 40–69 years.
• Limitations of mammography in developing countries are economic constraints and quality assurance.

• Cost effectiveness and false positives are the other limitations in the use of mammography in India.

• The decision to perform mammography should be determined with shared decision making about risks and benefits and by individual patient values.
Breast cancer and HT
No Consistency in Reporting

1975-2000       -------     45 Published Results

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Mrs S, a 55-year-old woman, presents at your clinic after several courses of antibiotic therapy with no relief. She was prescribed the treatment by a general practitioner for urogenital itching and irritation.

Chronic Tobacco use.

Her random blood glucose is within the normal range.

Dyslipaemia

BMI -35

She has been amenorrheic for past 3 years

Examination: Vaginal walls dry and atrophic

GP 2 with latent Risk
Management of Uro-genital Atrophy

- Risk assessment for cardiac disease- Therapeutic lifestyle management, treat dyslipaemia
- Vaginal estrogens Used daily for two weeks followed by bi-weekly for 3 months
- Vaginal lubricants can be recommended for subjective symptom improvement of dyspareunia
Urogenital Symptoms

- Vaginal ET is most effective for urogenital atrophy. Low dose vaginal preparations are as effective as systemic therapy. Some women on oral ET may require additional local therapy. Chronic therapy for atrophic vaginitis requires the use of the smallest effective dose; safety data from studies do not go beyond 1 year. Recurrent Urinary Tract Infection after ruling out other causes (GRADE A)
Urogenital Symptoms

- Progesterone supplement for endometrial protection is not needed along with the use of vaginal estrogen. (Grade C)
- Endometrial surveillance is not necessary in low risk asymptomatic woman
- Unscheduled bleeding should be investigated by an ultrasound and endometrial biopsy (Grade A)
- Conjugated equine estrogen (CEE) cream, estriol or estradiol cream, a low-dose estradiol tablet or a sustained-release intra-vaginal estradiol ring
Case-14

- Mrs G, a 51-year-old woman on continuous transdermal estrogen, natural progestogen therapy (EPT) for 4 months complains of intermittent spotting episodes
- The patient was prescribed EPT for management of hot flushes and night sweats
- She has been amenorrheic for 2 years
- Medical History:
  - BMI -30
  - G2P2A0
  - No H/O Hypertension
  - H/O Hyperlipidemia controlled with atorvastatin 10mg

GP 2 with risk factor
HT-VTE

Transdermal estradiol with micronised progesterone or dydrogesterone are preferred in women with risk for VTE
Endometrial Surveillance

- Not necessary in low risk asymptomatic woman
- Unscheduled bleeding should be investigated by an ultrasound and endometrial biopsy (Grade A)
- A thorough clinical examination is carried out to rule out cervical, vulval and vaginal cancer, atrophic vaginitis, urinary, and anal causes for bleeding
Endometrial Surveillance

- Women with PMB --- assessed initially with TVS, an endometrial biopsy (Grade A)

- Endometrial thickness is measured as the maximum anterior-posterior thickness of the endometrial echo on a long-axis transvaginal view of the uterus
Endometrial Surveillance

• Endometrial thickness of ≤ 4 mm in TVS do not require endometrial sampling unless they are at a high-risk for endometrial carcinoma or bleeding is episodic

• Endometrial thickness is > 4 mm on TVS --- endometrial sampling

• Endometrium thickness = 6 mm on TVS with homogeneous and normal morphology, women on HT and hypertensive medication is acceptable
Endometrial Surveillance

- A focal increased echogenicity or a diffuse heterogeneity in the endometrium even in a thin endometrium warrants further investigations.
- Out-patient endometrial sampling devices such as Pipelle and out-patient hysteroscopy can be carried out wherever possible.
Endometrial Surveillance

• Endometrial biopsy tissue is reported as insufficient, and endometrial thickness on TVS is less than 4 mm, follow-up is sufficient. Recurrent episodes warrant further investigations.

• Dilatation and curettage and fractional curettage are useful in low resource settings. Saline infusion sonography and 3D (USG) Ultrasonography play a limited role in PMB evaluation.
Mrs D, 57-year-old woman consults you with a query on her HT
She has been on cyclic EPT therapy for past 4 years after complete amenorrhea
It was prescribed to her for management of VMS and vaginal dryness
The therapy has been very effective with very few side effects
She has now decided to discontinue with HT
She wants to know the way forward

GP2 without disease
Duration of Use

» Natural menopause: Safety data of EPT therapy with CEE+P is 3–5 years with ET safety data for use is 7 years of treatment with 4 years follow-up

» Role of extended use of HT is a shared decision between the woman and the physician and may be considered in cases of recurrence of symptoms after stopping therapy, in cases of management of osteoporosis when other therapies are contraindicated (Grade A)

» Stopping HT: May be abrupt or the dose and duration may be tapered off gradually (Grade C)

HT: Hormone Therapy
MPA: Medroxyprogesterone Acetate
CEE: Conjugated Equine Estrogen
EPT: Estrogen Progestogen Therapy
Case 16

How do we manage cases of Abnormal Uterine Bleeding in Premenopausal Women With Breast Cancer with any of the following situations

• Menorrhagia?
• Symptomatic fibroids?
• Endometrial polyp?
• Endometrial hyperplasia, no atypia?
• Complex atypical hyperplasia?

**Group 2 with disease**

**HOW DO WE MANAGE?**
Case 17

- Mrs Vani 39 years, diagnosed as Ca Ovary stage I B, grade II clear cell carcinoma during diagnostic Laparoscopy for Infertility work up

- Frozen section, fluid analysis, TAH with BSO, omentectomy and staging lymphadenectomy done

- Post operative chemotherapy given
• Asymptomatic for menopausal symptoms

• High Risk for CVD
  - Mild Hypertension
  - on Atenolol 50mg
  - Raised triglycerides
  - Mother had stroke

• BMD - Normal Study

GP1 with disease
Issues

- Premature Menopause
- CVS
In Premature menopause—HT can be prescribed up to the natural age of menopause; further continuation of therapy is a shared decision between the woman and the physician according to the indication and the need (Grade C)
HT: Duration of Use

•Premature menopause- upto the natural age of menopause

•Natural Menopause- Safety data of EPT therapy with CEE +MPA is 3-5yrs, with ET safety data for use is 7yrs with a 4 yr follow up

•Stopping HT: May be abrupt or the dose and dosage tapered
Cardiovascular system -HT

Perception
• HT increases the risk of coronary heart disease (CHD) throughout the whole postmenopausal period

Evidence
• HRT in women aged 50-59 years does not increase CHD risk in healthy women and may even decrease the risk in this age group
• [A] Women within 10 years of menopause 0.89 where as it is 1.7 in women more than 20 years after menopause
Case 18

Mrs. M. 38 years

- C/O Six months amenorrhoea, hot flushes, sweating, palpitation, white discharge.
- P1A1; Fothergill’s surgery in 1994.
- H/o RA- on methotrexate, steroid-2yrs.
- H/O diabetes- since 1 year- Lifestyle modification
- Maternal Aunt- Breast cancer.

GP2 with disease
• CBP, Routine biochemistry, kidney function, lipid profile, S.calcium, Alkaline phosphate, Thyroid profile - Normal
• S.FSH - 45ng/ml
• RF - Positive
• U/S Pelvis - Endometrium- 4mm
• Mammogram - Dense Breasts
• Cervix - Biopsy(1994)- Moderate to severe dysplasia
• Pap’s smear - 2005- Mild dysplasia
  - 2006- inflammatory smear
  - 2007- Mild dysplasia
Course

• Not willing to take conventional HT
• Tibolone 2.5mg, calcium supplement—was this right approach?
• Three months later irregular bleeding
• Colposcopy, TVS- E-10mm, irregular echogenic spaces
• Color Doppler- Normal flow
• Hysteroscopy- Thick fibrous fundal adhesions
• EB- Blood clot, no tissue
• Cervix- Chronic nonspecific cervicitis

Problem

• Premature menopause, Rheumatoid arthritis
• Dense breasts
• Endometrial and cervical surveillance
Case –19

• Mrs. A. Age 57Yrs.

• Reached menopause 8 Yrs ago / 1 yr ago, Asymptomatic, BMI-26

• Complaint :- Pain both knee joints

• Diagnosis :- Investigation revealed osteoarthritis

GP1 with disease
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