MANAGEMENT OPTIONS
OBJECTIVE

Individualised specific care for women

At

Menopause Transition
EXPECTED OUTCOME

a) Primary preventions - life style modification, diet calcium and Vit D.

b) Understanding principles of symptomatic treatment

c) Medications used - inclusive of MHT
Presentation of patients

- No risk factors - healthy
- Healthy but Pt with risk factors -
- Already symptomatic but no medical problem
- Already with some medical problem
WHAT ARE WE GOING TO PREVENT?

- Over weight
- Metabolic syndrome
- CHD
- Osteoporosis
- Cancers
- Late sequelae
- Treat urogenital atrophy and vasomotor symptoms
MANAGEMENT

Lifestyle changes

- Avoidance of smoking & alcohol
- Diet & Exercise

Non hormonal

- Ca & Vit D supplements
- Bisphosphonates and others
- Phytoestrogens
Nutrition plan for an adult sedentary woman

<table>
<thead>
<tr>
<th>Food source</th>
<th>gm/day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cereals and millets</td>
<td>270</td>
</tr>
<tr>
<td>Pulses (vegetarian)</td>
<td>60</td>
</tr>
<tr>
<td>Non-vegetarian</td>
<td>30</td>
</tr>
<tr>
<td>Vegetables</td>
<td>300</td>
</tr>
<tr>
<td>Fruit</td>
<td>100</td>
</tr>
<tr>
<td>Sugar diary products</td>
<td>300</td>
</tr>
<tr>
<td>Fats and oils</td>
<td>20</td>
</tr>
<tr>
<td>Sugar</td>
<td>20</td>
</tr>
<tr>
<td>Salt</td>
<td>5</td>
</tr>
<tr>
<td>Water</td>
<td>8–10 glasses</td>
</tr>
</tbody>
</table>

The National Institute of Nutrition plan for an adult sedentary woman is a good strategy for healthy living.
## Common Indian Dietary Sources of Phytoestrogen

<table>
<thead>
<tr>
<th>Isoflavonoids</th>
<th>Lignans</th>
<th>Saponins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bengal gram</td>
<td>Linseed</td>
<td>Turmeric</td>
</tr>
<tr>
<td>Chick peas</td>
<td>Rye</td>
<td>Liquorice</td>
</tr>
<tr>
<td>Cherries</td>
<td>Millet</td>
<td>Ginger</td>
</tr>
<tr>
<td>Pareley</td>
<td>Bengal gram</td>
<td>Wild yam</td>
</tr>
<tr>
<td>Apples</td>
<td>All pulses</td>
<td>Fenugreek</td>
</tr>
<tr>
<td>Mung beans</td>
<td>Sesam and Sunflower seeds</td>
<td>Beet root</td>
</tr>
<tr>
<td>Whole grains</td>
<td>Legumes and beans</td>
<td>Root vegetables</td>
</tr>
<tr>
<td>Alfaalfa</td>
<td>Whole grains</td>
<td>Grains</td>
</tr>
<tr>
<td>Soya</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Red clover</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ref: Rao, B.S Narasinga: Bioactive phytochemicals in Indian foods. NFI Bull; 16(1) 1995: www.indianherbalremedies.com
Food containing phytoestrogen

- Carrot, Beets, Pumpkin, Potato, Red beans, Peas, Garlic, Egg plant, Tomato, Soya beans, Apple, Plum, Papaya, Pomegranate, Dates, Cherries, Cucumber, Par boiled rice, Oats, Barley, Wheat, Yam, Saunf.

- Fermented Foods like –
  - Idli, Dhokla

- Enhance the nutrient content of diets, esp. those which contain a cereal- pulse mix.

http://www.holistic-online.com/Remedies/hrt_food_and_estrogen.htm
The Recommended Dietary Allowance (RDA) of calcium intake for Adult Indian

<table>
<thead>
<tr>
<th>Group</th>
<th>Calcium (mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adult Women</td>
<td>600</td>
</tr>
<tr>
<td>Pregnancy</td>
<td>1200</td>
</tr>
<tr>
<td>Lactation</td>
<td>1200</td>
</tr>
<tr>
<td>Post-menopausal women</td>
<td>800</td>
</tr>
</tbody>
</table>

*Guidelines on Management Of Menopause 2013, Indian Menopause Society*
RDA of Calcium

- Assess the total calcium intake from dietary sources and if needed, supplements are used to correct the deficient balance. The intake should exceed >800 mg/day (Grade B). The risk of cardiovascular events, calculi are not observed with the recommended doses of calcium.

Guidelines on Management Of Menopause 2013, Indian Menopause Society
**Recommendation: RDA Vitamin D**  
**Guidelines on Management Of Menopause**  
**2013 Indian Menopause Society**

<table>
<thead>
<tr>
<th>Life Stage group</th>
<th>Daily Requirement</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infants (0-12 Months)</td>
<td>400–1000 IU</td>
<td>2000</td>
</tr>
<tr>
<td>Adults (1-18 year)</td>
<td>600-1000 IU</td>
<td>4000 IU</td>
</tr>
<tr>
<td>Age (19-50 year)</td>
<td>1500-2000 IU</td>
<td>10,000 IU</td>
</tr>
<tr>
<td>Age (50 &amp; Above)</td>
<td>1500-2000 IU</td>
<td>10,000 IU</td>
</tr>
<tr>
<td>Pregnancy &amp; Lactation (14-18 yr)</td>
<td>600-1000 IU</td>
<td>4000 IU</td>
</tr>
<tr>
<td>Pregnancy &amp; Lactation (19-50 yr)</td>
<td>1500 – 2000 IU</td>
<td>10,000 IU</td>
</tr>
</tbody>
</table>

*UL*: Upper Tolerable intake Level
Natural Source

- It is preferable to get vitamin D through sunlight by exposing 20% of body surface area (face, neck, and both arms and forearms) without sunscreen for at least 30 minutes between 10 am and 3 pm, depending on the season, latitude, altitude, pollution, and skin pigmentation.

- The sunlight between 11 am to 2 pm is preferably the best.

*Indian Menopause Society Guidelines on PMO 2013*
Management of Vit D Deficiency

- Cholecalciferol (vitamin D3) tablet or powder 60,000 IU/once a week for eight weeks preferably with milk or
- One IM injection of 6,00,000 IU is given to correct the deficiency. (not to be repeated before three months and may be given after confirmation of persisting low levels of vitamin D).
- Maintenance therapy (from natural sources or supplements) is advised after correction of the deficiency.

*Indian Menopause Society Guidelines on PMO 2013*
Maintenance Therapy

- Cholecalciferol tablet or powder 60,000 IU once a month in summer or twice a month in winter
- Vitamin D supplements by oral spray or oral tablets of 2,000 IU/day, or
- Injection of Cholecalciferol 3,00,000 IU IM, twice a year or 6,00,000 IU IM once a year.
- Cholecalciferol, 1,000 IU daily, will raise blood levels, on average, by approximately 10 ng/mL.

*Indian Menopause Society Guidelines on PMO 2013*
THE ROLE OF EXERCISE

Studies have shown that weight-bearing exercise lead to increased muscle mass and development of increased bone mass.
EXERCISE

- Minimum should be 30-45 mins, 4 times a wk
- Aerobic exercise for cardiovascular health
- Weight training/ resistance exercises for bone
- Health
- Yoga

*Guidelines on Management Of Menopause 2013 Indian Menopause Society*
EXERCISES

- Never too late
- Weight bearing
- Strength training
- Flexibility
- Back strengthening
- Balance
- Breathing exercises
- Brain exercises
Exercises

Stretching exercises

Resistance and weight bearing
MANAGEMENT OF HOT FLUSHES

- Loose cotton clothing
- Avoid warm drinks and hot baths
- Restrict alcohol, caffeine.
- Smoking cessation
- Diet & exercise, Paced Respiration, yoga
Paced Respiration Programme

Paced Respiration

- It's a technique using slow controlled, diaphragmatic breathing. In three randomized prospective trial, paced respiration decreased the frequency of hot flushes by 50%.

Treatments of VMS: Nonprescription Options

- Best studied options:
  - Soyextract\textsuperscript{a} and red clover isoflavones\textsuperscript{b}
  - Black cohosh\textsuperscript{b}
  - Chinese herbs\textsuperscript{c}

- None of these options have consistently been found more effective than placebo \textsuperscript{a-c}

- Trials comparing efficacy of nonprescription agents to HT→HT substantially more effective

\textsuperscript{a} LevisS, etal. \textit{Arch Intern Med.} 2011;171:1363-1369.
\textsuperscript{c} KaunitzAM. \textit{Menopause}. 2009;16:428-429.
PHYTOESTROGENS

- Naturally occurring phenolic compounds
- Weak oestrogenic action
- Indian diet rich in phytoestrogens
- Whole grain, all pulses, turmeric, ginger, beetroot, cabbage, beans, apples, soya
- Variation in plasma levels in individuals
PHYTOESTROGENS

- Hot flushes reduced by 40%
- Low prevalence of breast cancer in Japan
- Mortality from CHD low in Japan
- Lowers total cholesterol, LDL and triglycerides, no change in HDL
- Bone: Only small studies in humans
- More data in a few years
PHYTOESTROGENS

- Effects of soy foods is dose related
- Recommended intake is 40-50mg/day
- Isoflavone preparations less effective than soy foods
- Effects due to synergism
- Long term safety data not available
- In India not converted to EQUOL
Treatments for VMS: Prescription Therapy (Nonhormonal)*

- **Antidepressants**:†
  - SN RI: venlafaxine; desvenlafaxine
  - SSRI: paroxetine; fluoxetine

- **Gabapentin**

- **Clonidine**:†

  All reduced number and severity of hot flushes (compared with placebo).

* Represents off-label use.
† Reductions were significant compared with placebo

Treatments for VMS: Prescription Therapy (Hormonal)

- Estrogen used for many decades for VMS
- Most effective treatment
  - Numerous randomized, placebo-controlled trials
  - 75% reduction in VMS frequency
  - Significant reduction in VMS severity
- Oral and transdermal estrogen have similar efficacy

BEFORE PRESCRIBING MHT

- Dialogue and documentation
- Medical conditions and risks should be identified
- Pre HT tests conducted
- Individualised dose, duration and follow up
- Addition of progestogens - Intact uterus, endometriosis, stage I & II endometrial CA and Supracervical hysterectomy in hysterectomised women
- Offer hormone therapy, if not contraindicated

Guidelines on Management Of Menopause
2013 Indian Menopause Society
INITIAL SCREENING

- History taking
- Examination:
  - General
  - Height, Weight, Waist Circumference
  - Pelvic
  - Breast exam

Guidelines on Management Of Menopause
2013 Indian Menopause Society
INITIAL SCREENING

- Complete blood count, Urine routine.
- Fasting glucose level.
- Lipid profile.
- Serum TSH.
- Stool for occult blood.
- PAP smear.
- Transvaginal ultrasound.
- Mammogram/ultrasound.
- Eye checkup – intraocular pressures, refractive index, and retina.

Guidelines on Management Of Menopause
2013 Indian Menopause Society
### Mid Life OPD cards

**Name of Dr.:**

**Address of Dr.:**

**S.No.:**

**Patient Name:**

**Age:**

**Address of Patient:**

**Religion:** Hindu / Sikh / Christian / Muslim

**Ph. Mobile:**

---

<table>
<thead>
<tr>
<th><strong>PERSONAL DETAILS</strong></th>
<th><strong>PAST HISTORY</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Name:</td>
<td>NIDDM</td>
</tr>
<tr>
<td>Age:</td>
<td>Hypertension</td>
</tr>
<tr>
<td>Menarche (age 1)</td>
<td>Heart problem</td>
</tr>
<tr>
<td>Menopause (age 2)</td>
<td>Fragility fracture</td>
</tr>
<tr>
<td>Marital status:</td>
<td>Rheumatoid arthritis</td>
</tr>
<tr>
<td>Menstrual formula:</td>
<td>Cancer breast</td>
</tr>
<tr>
<td>Obstetric history:</td>
<td>Cancer ovary</td>
</tr>
<tr>
<td>Address &amp; mail:</td>
<td>Any other cancer</td>
</tr>
<tr>
<td></td>
<td>Thrombembolic phenomenon</td>
</tr>
<tr>
<td><strong>Email id:</strong></td>
<td>Asthma / thyroid disorder / gall stones</td>
</tr>
<tr>
<td><strong>Mobile number:</strong></td>
<td>Eye problem</td>
</tr>
<tr>
<td><strong>Emergency contact number:</strong></td>
<td>Joint ache and pain</td>
</tr>
<tr>
<td>Allergic to (please specify, if any):</td>
<td>Hot flushes</td>
</tr>
<tr>
<td></td>
<td>Mood disturbances</td>
</tr>
<tr>
<td><strong>LIFESTYLE HISTORY</strong></td>
<td>Womental problems</td>
</tr>
<tr>
<td>History of alcohol intake &gt; 2 drinks:</td>
<td>Healing loss</td>
</tr>
<tr>
<td>Smoking:</td>
<td>Memory loss/ailments</td>
</tr>
<tr>
<td>Caffeine:</td>
<td></td>
</tr>
<tr>
<td>Exercise:</td>
<td></td>
</tr>
<tr>
<td>Diet calcium:</td>
<td></td>
</tr>
<tr>
<td>Vitamin D intake:</td>
<td></td>
</tr>
<tr>
<td>Medication history if any:</td>
<td></td>
</tr>
<tr>
<td>Special Intake if any and doses:</td>
<td></td>
</tr>
</tbody>
</table>

---

<table>
<thead>
<tr>
<th><strong>FAMILY HISTORY</strong></th>
<th><strong>BASE LINE INVESTIGATIONS</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>NIDDM</td>
<td>Hemoglobin</td>
</tr>
<tr>
<td>Hypertension</td>
<td>Lipid profile</td>
</tr>
<tr>
<td>Heart problem</td>
<td>[HDL] [CHOLESTEROL TOTAL]</td>
</tr>
<tr>
<td>Fragility fracture</td>
<td>TSH</td>
</tr>
<tr>
<td>Rheumatoid arthritis</td>
<td></td>
</tr>
<tr>
<td>Cancer breast</td>
<td>[TROGYRIDES] [LDL]</td>
</tr>
<tr>
<td>Cancer ovary</td>
<td>TSH</td>
</tr>
<tr>
<td>Any other cancer</td>
<td>[BMD T1Z SCORED]</td>
</tr>
<tr>
<td></td>
<td>Pap smear [HRG] [HPV] [HR]</td>
</tr>
<tr>
<td><strong>GENERAL PHYSICAL EXAMINATION</strong></td>
<td>Ultrasound</td>
</tr>
<tr>
<td>Physical:</td>
<td>[Mammography]</td>
</tr>
<tr>
<td>Height:</td>
<td></td>
</tr>
<tr>
<td>Weight:</td>
<td></td>
</tr>
<tr>
<td>BMI:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>BP:</td>
<td></td>
</tr>
<tr>
<td>WHR / WAIST HIP / WRIST:</td>
<td></td>
</tr>
<tr>
<td>Gait:</td>
<td></td>
</tr>
<tr>
<td>Any other:</td>
<td></td>
</tr>
<tr>
<td><strong>LOCAL EXAMINATION</strong></td>
<td></td>
</tr>
<tr>
<td>Breast:</td>
<td></td>
</tr>
<tr>
<td>Vagina:</td>
<td></td>
</tr>
<tr>
<td>Pro:</td>
<td></td>
</tr>
<tr>
<td>PV:</td>
<td></td>
</tr>
<tr>
<td>Gynae T/V:</td>
<td></td>
</tr>
<tr>
<td>General:</td>
<td></td>
</tr>
</tbody>
</table>
GUIDE TO LIVE HEALTHY LIFE LONG & ALWAYS

DIET
Calcium Intake: 1200-1500 mg daily
VIT D: 400-800 IU/day

Blood Indicators
Hemoglobin Level: 12 Gm% - 15 Gm%

Exercise
Aerobic Exercise: 30 Minutes 5 times a week, Weight Bearing/Resistance Exercise: 20 Min/day, 2-3 Days a week

Vital Stats
WHR (Waist Hip Ratio: 0.8 Women) or absolute 34 inches, BMI 19-25 ideal

BREAST CANCER SCREENING
- Breast self-examination
- Clinical examination - every year
- Mammography - more than 40 years age - every 2 years

MENOPAUSE RATING SCALE
- Hot flashes, sweating (episodes of sweating)
- Heart discomfort (unusual awareness of heart beat, heart skipping, heart racing, tightness)
- Depressive mood (feeling sad, down on the verge of tears, lack of drive, mood swings)
- Irritability (feeling nervous, irritable, tension, feeling aggressive)
- Anxiety (involuntary restlessness, feeling panicky)
- Sexual problems (change in sexual desire, activity and satisfaction)
- Physical and mental exhaustion (general decrease in performance, impaired memory, decrease in concentration, forgetfulness, fatigue, headache, discomfort)
- Bladder problems (difficulty in urinating, increase in frequency, bladder incontinence)
- Dryness of vagina (sensation of burning or dryness in vagina, difficulty in sexual intercourse)
- Joint & muscular discomfort (joint pain, muscle pain, backache)

According to WHO standards, the degree of severity are consistent with

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Degree of Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>No problem/None</td>
<td>absent negligible</td>
</tr>
<tr>
<td>Mild problem</td>
<td>slight low</td>
</tr>
<tr>
<td>Moderate problem</td>
<td>medium low</td>
</tr>
<tr>
<td>Severe problem</td>
<td>high extreme</td>
</tr>
<tr>
<td>Complete problem</td>
<td>total</td>
</tr>
</tbody>
</table>

According to WHO standards, the degree of severity are consistent with

<table>
<thead>
<tr>
<th>Symptom</th>
<th>Degree of Severity</th>
</tr>
</thead>
<tbody>
<tr>
<td>No problem/None</td>
<td>absent negligible</td>
</tr>
<tr>
<td>Mild problem</td>
<td>slight low</td>
</tr>
<tr>
<td>Moderate problem</td>
<td>medium low</td>
</tr>
<tr>
<td>Severe problem</td>
<td>high extreme</td>
</tr>
<tr>
<td>Complete problem</td>
<td>total</td>
</tr>
</tbody>
</table>

Academic Partner
Abbott Nutrition

The Trademark of Abbott Group of Companies

Indian Menopause Society
MENOPAUSAL HORMONE THERAPY

- Conventional
  - Oestrogen alone
  - Oest & Prog: Continuous combined Sequential

- STEAR: Tibolone

- SERMS: Raloxifene

- TSEC: Bazedoxifene + Conjugated Estrogen
How is HRT Given?

**Continuous Estrogen**
- Estrogen
- No tablet break
- No bleeding as no uterus

**Continuous Sequential HRT**
- Estrogen
- Progestogen
- Day 14
- Sequential therapy without tablet break
- Regular bleeding at end of cycle

**Continuous Combined HRT**
- Estrogen
- Progestogen
- Day 14
- Combined therapy without tablet break
- No bleeding at end of cycle
MECHANISM OF ACTION

- Estrogens act only as agonists via E2 receptors
- STEAR: Tibolone acts via E2 receptors agonistically & tissue selectivity is achieved via enzyme regulation
- SERMS act via E2 receptors being agonistic or antagonistic on different tissues
ROUTE OF ADMINISTRATION

- Oestrogen
- Oral, Transdermal, Vaginal
- Progestogen
- Oral, Vaginal, Intra-uterine
OESTROGEN

- Reduces vasomotor symptoms & insomnia
- Increases bone mineral density
- Lowers Cholesterol & LDL (Oral Oestrogens)
- Increases HDL (Oral Oestrogens)
- Reduces vaginal dryness
- Decreases dyspareunia
- Increases Triglyceride
OESTROGEN PREPARATIONS

- Oral
- CEE : 0.3, 0.625
- Estradiol valerate : 1, 2mg
- Transdermal
OESTROGENS- SIDE EFFECTS

Problems

- Breast tenderness – especially in those over 60
- Fluid retention
- Nausea
- Heavy withdrawal bleeds
- Breakthrough bleeding
- Endometrial hyperplasia
OESTROGENS

SIGNIFICANT ADVERSE EFFECTS

- Breast cancer if used more than 5-7 yrs Estrogen alone does not increase incidence
- Endometrial cancer if E+P then no increased incidence
- Venous Thromboembolism can be given TD or progesterone
- Stroke perhaps dose related
Management of the Patient with Persistent Symptoms

**Treatment**

- Alter dose of estrogen
- Change type of estrogen formulation or route of administration
- Decrease dose of frequency of progestogen
- Change type of progestogen formulation
- Change time of medication administration
- Add additional nonhormonal medication
**PROGESTOGEN**

- Should be added to systemic estrogen for all women with a uterus to prevent endometrial hyperplasia and cancer.

- Low-dose vaginal estrogens, administered for the relief of urogenital atrophy, are systemically absorbed, but not at levels that stimulate the endometrium, and so concurrent progestogen is not required. Studies are for one year only.
PROGESTOGEN

- Micronised progesterone
- LNG-IUS
- Provides adequate endometrial protection
- Drospirenone
- Anti-androgenic & anti-mineralocorticoid
- Hypertension
PROGESTOGEN

- MPA : 2.5 mg daily, 5 mg x 12 days/mth
- NETA : 0.5 mg daily, 1 mg x 12 days/mth
- Micronised progesterone
  - Oral 200 mg daily, 300 mg x 12 days/mth
  - Vaginal 100 mg daily, 200 mg x 12 days/mth
- Dydrogesterone : 10 mg x 12 days/mth
- Drosperinone : 0.5 mg daily(with E2 1mg)-NA
PROGESTOGEN- SIDE EFFECTS

- Edema, weight gain, bloating, migraine
- Acne, greasy skin, hirsutism, negative mood changes
TIBOLONE

- STEAR
- Oestrogenic action on bone, vagina, vasomotor symptoms and lipids
- Progestogenic & antiestrogenic action on endometrium and breast
- Androgenic action on mood and libido
TIBOLONE

SPECIFIC INDICATIONS

- Mood & libido
- Adverse effects with conventional MHT
- Older women
- Family history of breast cancer
- History of endometriosis
- Add back therapy with GnRH analogues
TIBOLONE

- 2.5 mg single daily dose orally
- 1.25 mg equally effective

ADVERSE EFFECTS

- Nausea & weight gain
- No change in HDL level
- Increases risk of recurrence in breast cancer survivors
RALOXIFENE - ACTIONS

- Oestrogen agonist on bone and heart
- Antagonist on breast and uterus
- No relief in vasomotor symptoms
- Does not relieve vaginal dryness
SERMS- RALOXIFENE (EVISTA®)

Raloxifene

- Non-steroidal benzothiopene – binds Estrogen receptor, Inhibits bone resorption without stimulating endometrium
- Multiple Outcomes of Raloxifene Evaluation (MORE)

- Studied 60 mg and 120 mg doses on patients with and without VCF (vertebral clinical fracture)
- 2.6% ↑ BMD compared to placebo
- 30% (prior VCF) and 50% (no prior VCF) reduction in VCF
- RR of DVT = 3
- Significant reduction in incidence of breast CA

Side effects are hot flushes can be given only postmenopausal
RALOXIFENE
SPECIFIC INDICATIONS

- Osteoporosis
- Older women
- Family history of breast cancer
- Treated breast or endometrial cancer
RALOXIFENE

- Used as single daily dose of 60mg orally
- Initiate therapy at least one yr after menopause

**Adverse Effects**

- Increases hot flushes
- Leg cramps
- Venous thrombo-embolism
- Caution in non-ambulatory women
TSEC

- Tissue Selective Estrogen Complex
- Combination of a SERM with Estrogen
- To provide efficacy of both components
- Fewer adverse effects
- Rationale is that tissue selective activity
- Blended activities of SERM and Estrogen
- Bazedoxifene (BZA) with Conjugated Estrogens (CE)
SMART- 1- 5

- BZA 20 mg/CE 0.45 mg
- Treat menopausal symptoms and postmenopausal bone loss without stimulating the endometrium
  Amenorrhoea & breast pain
- Safety : Mild adverse effects
- Endometrial hyperplasia > in BZA 10 mg
- VTE, MI : No diff bet all doses & placebo
- Approved in US this yr, filed for approval in UK & EU
Selected Bisphosphonates
(tablet administration)

- Alendronate (Fosamax®)
- Risedronate (Actonel®)
- Etidronate (Didronel®)
- Tiludronate (Skelid®)
BISPHOSPHONATES

Adverse effect

- Poor intestinal absorption
- N2 – containing
- GI upset
- Oesophagitis
- Patient should remain upright, take with a glass of water
Alendronate (Bishphonate)

- Non hormonal
- FDA approved
- For prevention as well as treatment
- Increases BMD by 8.8% in lumbar spine and 6% in fracture NOF
- 48% reduction in # NOF and spine fractures
- Can be given for 5-10 yrs or treatment free holidays can be given.
DOSE: daily or weekly

Except – very elderly and poor renal function

PREVENTION: 5mg per day, 35 mg /week
Treatment: 10 mg/day, 70 mg/week

CARE

- Empty stomach consumption
- Calcium to be taken after 4 hrs
- Longest duration tried – upto 5 yrs
ZOLEDRONIC ACID

- Inj ACLAST I/V 5 mg in 100 ml
RISEDRONATE (ACTONEL®)

The Vertebral Efficacy with Risedronate Therapy (VERT) Study

- North American and Multinational Arms
- Randomized, double-blind, placebo-controlled study of 2458 postmenopausal women with ≥1 VCF
- Treatment with 5mg/day for 3 years:
  - ↓ incidence of new VCF by 41%
  - ↑ BMD 5.4% vs. 1/1% (placebo)
CALCITONIN

Prevent Recurrence of Osteoporotic Fracture Study (PROOF)

• 5-yr, multicenter, double-blind, randomized study – 1255 patients
  • 817 pts c 1-5 previous VCF
  • Nasal spray salmon calcitonin (100, 200, 400 IU)
  • 36% reduction in VCF (33% for entire group)
  • Lumbar BMD ↑ 1.2% during only 1st yr
CALCITONIN

- Analgesic Effects
  - Analgesic for acute and chronic pain of VCF
  - Apparent by = 1 week
  - Mechanism likely a central effect (hypothalamus, PAG, dorsal horn)

- Side Effects
  - Minimal: rhinitis, back/joint pain, HA

- Resistance
  - Antibodies in 20% PROOF patients
CALCITONIN

INJECTABLE – 100 IU/day s/c BIOCALCIN
NASAL SPRAY 200 IU /day MIACALCIN

- Inhibits osteoclast
- Increases BMD by inhibiting osteoclast, decrease vertebral fractures
- Good for pain in spinal fractures
ANABOLIC AGENTS

- PTH
- Fluoride
- IGF-1
- Strontium (PREVOS- / SOTI (sp.OsteoporosisTherapeutic Intervention)/ TROPOS (treatment of post menopausal osteoporosis) g both a mild anabolic effect and a mild antiresorptive effect on bone tissue (Marie et al 1993; Canalis et al 1996)
- Tibolone
- Statins
PTH

- Forteo
  - Teriparatide = generic name
  - Synthetic teriparatide has been used in many clinical trials
  - Forteo is the recombinant DNA PTH 1-34 manufactured by Eli Lilly
  - Genetically engineered fragment of native PTH (84 amino acids)
  - FDA approved in US and Europe
    - 24 month treatment period
    - $600/month
  - A Recombinant DNA prep with all 84 amino acids (Preos) in clinical trials
PTH (Forteo)
Neer et al. (2001) NEJM 344(19), 1434-1441

- Landmark Placebo controlled, randomized trial of 1637 postmenopausal women with prior vertebral fracture
  - 20µg vs 40µg Forteo
  - RR VCF = 0.35 for 20µg dose and 0.31 for 40µg
  - Lumbar spine BMD - ↑ 9%
  - Femoral neck BMD - ↑ 3%
  - Distal radius BMD - ↓ 2%
PTH (Forteo)

- **Side Effects**
  - Hypercalcemia (rare clinical significance)
  - Leg cramps, dizziness
  - Dose dependent increase in osteosarcoma in rats
  - None in 2000 Forteo patients

- **Contraindications**
  - Patients with open epiphysis
  - Paget disease
  - Prior skeletal malignancy
  - Metabolic bone diseases
  - Pre-existing hypercalcemia (Primary hyperparathyroidism)
New Drug Denosumab

Denosumab is a fully human monoclonal antibody to the receptor activator of nuclear factor-κB ligand (RANKL) that blocks its binding to RANK, inhibiting the development and activity of osteoclasts, decreasing bone resorption, and increasing bone density.
Dose of Denosumab

- Denosumab given 60 mg subcutaneously twice yearly for 36 months associated with reduced risk of vertebral, nonvertebral and hip fractures in postmenopausal women with osteoporosis

- Inj Prolia
FOLLOW UP

- Review after one month for efficacy and side effects
- After 3 months to assess effects & compliance 6 monthly for first year, then annually
FOLLOW UP INVESTIGATIONS

- Baseline investigations annually or earlier:
  - Routine blood and urine examination
  - Blood sugar
  - Lipid profile

- Pelvic USG, Mammography

- Pap Smear every 3 years

- DEXA once in two - five years [optional]

- Biochemical bone markers

*Guidelines on Management Of Menopause*

*2013 Indian Menopause Society*
An appealing alternative strategy is the use of a tissue-specific estrogen complex (TSEC). TSECs combine an estrogen and a SERM, taking advantage of the tissue-specific anti-estrogenic properties of the SERM in order to counteract the effects of estrogen on the uterus and breast. This combination, therefore, requires no progestogen.

MANAGEMENT OF URO-GENITAL ATROPHY

- Vaginal estrogen
- Used daily for one week, foll by bi-weekly for 3 months
- Estriol and CEE cream
- Estradiol tablet
Nonhormonal Treatment of WA

Behavioral
- Regular sexual activity can help

Nonhormonal therapies: excellent efficacy
- Moisturizers
  - Used daily
- Lubricants
  - Used during sexual activity

Johnston SL, et al. 
Strategies to Improve Patient Communications About Genital Atrophy

- **Ask directly:**
  - “Some women notice that they experience vaginal dryness at this time of life; are you experiencing discomfort with sexual activity?”

- **Consider that relationship/sexual issues may present as vaginal discomfort**
CASE

- 48 yr old, asymptomatic
- Getting regular periods
- Wants to know what medication to take to avoid problems of menopause

How will you counsel her?

- Lifestyle, diet, exercise, Ca and Vit D Supplements, Screening tests
EXERCISE AND FITNESS

What advice can we give our patients?
DIET IN MENOPAUSE

What are the recommendations?
CASE

- 50 yr, Para 1 presents with c/o recurrent urinary infections
- Amenorrhoea since 18 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
- Gen & Syst Exam : NAD
- P/S : Vagina atrophic
- P/V : NAD
- Provisional Diagnosis?
- Differential Diagnosis?
- Investigations?
**Results**

- **Hb**: 12 gm%  
- **WBC**: 7,000  
- **Plt**: 210  
- **BSL(F)**: 165 mg%, **(PP)**: 270 mg%  
- **Urine RE**: NAD  
- **TSH**: 16 uIU/ml  
- **FSH**: 48 IU/L  
- **USG**: Uterus normal size, endo 4mm, ovaries 2.1x3x2 cm and 2x3x2.4 cm
Treatment?

- Endocrine reference
- Control BSL
- Treat Hypothyroidism
- Vaginal estrogen creams
**GUIDELINE**

- ET is most effective treatment for symptoms of vaginal atrophy
- Vaginal ET recommended when HT is considered solely for this indication
- Vaginal ET benefits women with urge incontinence & reduces risk of Recurrent

*Guidelines on Management Of Menopause*
*2013 Indian Menopause Society*
CASE

- 46 yr old, C/o Hot flushes & night sweats, feeling low since 6 months
- Last period 2mths ago, 1-2/30-90days
- BMI : 30, BP : 150/100
- Investigations?
- Chol:280, LDL:165, HDL:34 Trig:190
- Management options?
● Lifestyle modification
● Statins
● SSRI, SNRI
● Clonidine
● Phytoestrogens
● HT ?
● Route of administration?
GUIDELINE

- Estrogen may have a protective role in CHD prevention in women aged 50-59 yrs
- Treating hypertension reduces risk
- Reducing obesity, improving diet & regular exercise are key measures

Primary Prevention of Coronary Heart Disease in Women
British Menopause Society Council Consensus Statement 2007
Answer True or False about the effect of Oral Oestrogen on lipid profile

1) Increases Triglycerides
   True

2) Increases Cholesterol
   False

3) Decreases LDL
   True

4) Decreases HDL
   False
A 55 year old with persistent urogenital symptoms inspite of oral HT, how do you manage?

1. Alter the dose, type or route of oestrogen
2. Alter the type and dose of progestogen
3. Add vaginal preparation
THANK YOU!
RALOXIFENE AND BREAST

- Antagonistic action
- No mastalgia
- Reduces risk of invasive cancer by 76%
- Reduces risk of ER positive cancer by 90%