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# QUARTERLY MEDICAL REVIEW

Vol. 60, No. 1

January - March 2009

**Review : Health of women over 40**  
(with special reference to postmenopausal symptoms, osteoporosis)



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## Health of Women over 40 (with special reference to Postmenopausal Symptoms, Osteoporosis)



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## ***Message from Dr Duru Shah***



### **Dear Friends**

**I** took over as President of the Indian Menopause Society on 16th March 2008. With the focus being on the ageing woman, the theme for this year has been suitably titled as "Better care in her changing world".

IMS has been an Organization in existence since 1995. It is an Organization with a difference. The difference being that it brings together not only gynecologists who are responsible for women's health, but also members from allied specialities such as orthopedics, rheumatology, endocrinology, dermatology, oncology and associated professions such as public health, social sciences, physiotherapy, etc. With such a varied membership, there are varied areas of interest, which makes this Organization so very unique. Woman's health is looked at in its entirety and not microscopically focused only on her reproductive system!

IMS is an organization which focuses on women's health both in the perimenopause and postmenopausal eras. It is affiliated to the International Menopause Society, the North American Menopause Society and the Asia Pacific Federation of Menopausal Societies. The Indian Menopause Society has at present 25 chapters nationwide with about 1500 members.

Human beings are living longer today to a large extent because of the medicine we practice. And women are outliving their male counterparts! As society ages, there are millions of women in the ageing group who require attention. It has to be such a wholesome attention that it gives them a quality life with dignity and meaning. What is achieved by just existing if one does not have the physical or mental capacity to live? What is the value of a life which is wasting immobilized on a bed with multiple fractures due to osteoporosis? We fail to find answers to such questions. My only answer is prevention.

As gynecologists we are practically the primary care physicians for women. It is our responsibility to offer preventive healthcare which is holistic. Besides preventing cancer of the reproductive tract through papsmear, pelvic ultrasound and mammography, we also prevent osteoporosis and cardiac disasters in the high risk groups.

In the last decade what has been upper most in my mind has been the preventive aspect of women's health. Today, science has taken us far ahead and we are able to treat most gynecological and obstetric problems either medically or surgically. It is time for us now to concentrate on preventive health care in order to give a better tomorrow to our women. Being a Society focused on the health of the mature woman, our entire focus should be on preventive healthcare, promising a better care for the woman in this new phase of her life. Better care in order to prevent the

disability, the cancer, the burden and the stress of life in her future and to give her the dignity and quality of life she deserves in her older age.

But how many of our women have the benefit of such care? In India we have 1,30,000 new cases of cervical cancer annually - which is 1/4th of the total new cases which occur in the world every year! 74,000 die annually from the disease, and in India, 24% of all cancers are in women.

- 50% Indian postmenopausal women have osteoporosis! Of all the fractures which occur, postmenopausal osteoporosis is the commonest and most preventable!
- Cardiovascular disease has been projected as the largest cause of death and disability in India by 2020! CVD leads to more deaths in women than cancer, HIV or malaria combined! Somehow CVD is primarily considered as a male disease and women are neglected for such health care.

We need to make our policy makers aware of this group of women. Unfortunately there is no organized program in India to prevent this huge burden of chronic diseases among women. There is a need to frame such policies that will deal with these problems more effectively. And it is for us to make this happen!

We can make it happen by creating a noise about these issues, by writing articles in newspapers and magazines, by discussions on radio or TV, through popular websites, by organizing camps and walks, by distributing educational booklets or pamphlets, by media campaigns and by advocacy with the Government.

I would like to give the following example of how each one of us can do our bit to give her "better care in her changing world"

*The Oyster .... Anonymous*

*There was once an oyster whose story I tell*

*Who found that some sand was inside his shell*

*Just one little grain, but it gave him great pain*

*For oysters have feelings, though they all seem so plain.*

*Now did he complain or blame his fate,*

*Which led him to such a deplorable state?*

*Did he curse out the Government - call for an election?*

*And cry that the sea "should have given protection?"*

*No! He said to himself as he lay on the shelf,*

*"Since I cannot remove it , I'll try to improve it  
The years rolled along as years always do  
And he came to his ultimate destiny - oyster stew!  
And the small grain of sand that had bothered him so  
Was a beautiful pearl, all richly aglow!  
The tale has a moral, for isn't it grand  
What an oyster can do with a morsel of sand ?  
What couldn't we do if we'd only try  
To prevent suffering, before women die!*

I thank Dr Reena Wani for inviting me to write this message for the following article on Menopause.  
I wish her all the best.

**Dr Duru Shah**  
**President**  
**Indian Menopause Society**

## **MENOPAUSE MANAGEMENT :**

***" TO TREAT OR NOT TO TREAT, THAT IS THE QUESTION!!!"***

**Dr. Reena J. Wani**

### **Introduction**

The term "menopause" comes from the Greek words meno (month) and pause (to end). Thus, it basically means permanent physiological, or natural, cessation of menstrual cycles. The absence of menstrual periods for 12 months is usually used as the clinical definition of "natural" menopause.

The word is commonly used in regard to women, where menopause happens more or less in midlife, signaling the end of the fertile phase of a woman's reproductive life. Menopause in women cannot however simply be defined as the permanent "stopping of the monthly periods", because in reality what is happening to the uterus is quite secondary to the process. For medical reasons, the uterus is sometimes surgically removed (hysterectomy) in a younger woman, and after this her periods will cease permanently and the woman will technically be infertile, but as long as her ovaries (or one ovary) are, or is, still functioning, the woman will not be in menopause. This is because even without the uterus, ovulation, and the release of the sequence of reproductive hormones that are an essential part of the reproductive cycles, will continue until the time of menopause is reached.

Menopause is in fact triggered by the faltering and shutting down (or surgical removal) of the ovaries, which are a part of the body's endocrine system of hormone production, in this case the hormones which make reproduction possible and influence sexual behavior.

The process of the ovaries shutting down is a phenomenon which involves the entire cascade of a woman's reproductive functioning, from brain to skin, and this major physiological event usually has some effect on almost every aspect of a woman's body and life.

### **Age at menopause and the "Menopausal Transition"**

The average age of menopause is 51 years old. But there is no way to predict when an individual woman will enter menopause. The age at which a woman starts having menstrual periods is also not related to the age of menopause onset. Most women reach menopause between the ages of 45 and 55, but menopause may occur as earlier as the 30s or 40s or may not occur until a woman reaches her 60s. As a rough "rule of thumb," women tend to undergo menopause at an age similar to that of their mothers.



Mean age at menopause ranges in Indian women from 40.32 to 48.84 years and in developed countries from 48.0 to 51 years. As menopausal health demands priority in Indian scenario due to increase in life expectancy and growing population of menopausal women, large efforts are required

to educate and make these women aware of menopausal symptoms. This will help in early recognition of symptoms, reduction of discomfort and fears and enable to seek appropriate medical care if necessary.

**Perimenopause** means "around the time of menopause." It is not officially a medical term, but is sometimes used to explain certain aspects of the menopause transition in lay terms. Perimenopause is different for each woman. In this stage women begin to experience the symptoms of menopause even though they are still experiencing ovulation and having menstrual periods. In this phase hot flashes and irregular periods begin to occur but it may be four to five years before full menopause sets in. It can begin up to 10 years prior to the last menstrual period.



During perimenopause, the production of most of the reproductive hormones, including the estrogens, progesterone and testosterone, diminishes and becomes more irregular, often with wide and unpredictable fluctuations in levels. During this period, fertility diminishes.

The actual duration and severity of perimenopause in any individual woman cannot be predicted in advance or during the process. Not every woman experiences symptoms during perimenopause. Approximately one third of all women get no noticeable symptoms other than that their periods become erratic

and then stop. Another one third of women have moderate symptoms. The remaining one third of women have very strong symptoms which tend to have a longer duration. The tendency to have a very strong perimenopause may be inherited in some cases.

**Premenopause** is a word used to describe the years leading up to the last period ever, when the levels of reproductive hormones are already becoming lower and more erratic, and symptoms of hormone withdrawal may be present.

**Postmenopause** is the entire period of time that comes after the last menstrual period. When twelve months have passed with no menstrual periods occurring, a woman has reached full menopause. The ovaries produce significantly less estrogen and progesterone and no longer release eggs; consequently pregnancy is no longer possible.

Any period-like flow that might occur during post-menopause, even just spotting, must be reported to a doctor. The cause may be minor, but the possibility of endometrial cancer must be checked for and eliminated.

### **Changes in the body after Menopause**

After menopause there are chronic conditions that tend to appear in women. Declining estrogen levels increase the risk of cardiovascular disease. To combat this potential risk, women should stop smoking, reduce their blood pressure, exercise regularly, and eat a diet rich in fruits, vegetables, and whole grains but low in saturated fats.

Bone density decreases at a rapid rate after menopause and some women develop osteoporosis. In this condition brittle, weak bones break easily, especially those in the hip, wrist, and spine. Adequate amounts of calcium at the rate of 1500mg a day as well as 400-800mg of Vitamin D will help to decrease this risk as will strength training and walking or jogging.



### **Symptoms and signs of menopause**

Menopause manifests at different times and in different ways for individual women. Some are lucky enough to get through the experience with no significant problems but for others, menopause disrupts both their lives and their interpersonal relationships.

There are a number of signs and symptoms to indicate the onset of menopause beginning with irregular menstrual periods. The irregularity may be apparent with increased or decreased frequency or in the amount of flow present. As ovulation begins to fluctuate, a woman is less likely to get pregnant but conception is still possible unless menstrual periods have been absent for a year.

Both the lining of the vagina and of the urethra become drier, thinner, and have less elasticity with the onset of menopause. Consequently women tend to experience burning and itching and have an increased chance of urinary or vaginal infections. A frequent urge to urinate is common with minor incontinence especially when laughing, sneezing, or coughing. (These problems can continue after full menopause.) In addition, sexual intercourse may become increasingly uncomfortable, even painful.

One of the most common menopause symptoms, the hot flash, is a consequence of dropping estrogen levels that cause blood vessels to expand rapidly with an attendant increase in skin temperature. Generally women experience sweating and flushed appearance. This can last from 30 seconds to several minutes and can occur as often as once an hour.

Although hot flashes can occur at any time of the day or night, night sweats are a related problem that severely disrupt the sleep cycle. Women report waking up from a deep sleep to find their night clothes and bedding soaked with sweat.

Most women gain some degree of weight during the onset of menopause, usually an average of five pounds. The increased weight concentrates around the waist and abdomen. Other changes in appearance can include fullness of the breasts, thinning hair, wrinkles, adult acne, and coarse hair (usually on the chin, upper lip, and sometimes on the chest and abdomen).

### **Diagnosis of menopause**

For the most part women are simply adequately attuned to their bodies to know when signs of menopause begin to appear. Typically irregular periods or hot flashes are the common presenting symptoms. However some women may not have any symptoms at all. Often it is a retrospective diagnosis with absent periods for a year. A progesterone challenge test is sometimes useful for a woman with secondary amenorrhea where we are suspecting declining ovarian function to be the cause of absent periods. If a woman over 40 years fails to menstruate with progesterone, and the

urine pregnancy test is negative, it is usually menopause.

In case blood tests are needed, usually levels of follicle-stimulating hormone and estrogen are estimated. FSH increases and estrogen decreases at the onset of menopause. Sometimes, a thyroid test may be in order as hypothyroidism can cause some of the same symptoms as menopause.

### Menopause Management: Overview

Over the past few decades there has been a paradigm shift in the approach to menopause, both from the provider and patient point of view. With increasing longevity and quality of life issues,



there was a shift from prescribing postmenopausal estrogen short-term (6 months-up to 5 years), to prescribing it long-term (more than 5 years) for prevention of disease, specifically coronary heart disease (CHD) and osteoporosis. However currently available clinical trial data, while confirming that estrogen prevents bone loss and fracture, does not confirm a positive effect on the heart at least with a continuous combined EP regimen. Data from the WHI and HERS (Heart Estrogen/ Progestin Replacement Study) trials suggest that continuous combined therapy with conjugated estrogen (0.625mg/ day) and medroxyprogesterone acetate (2.5 mg/day) is ineffective for

either primary or secondary prevention of CHD, and in fact slightly increases risk when used for primary prevention. <sup>(1)</sup>

The current recommendations of most groups, such as US Preventive Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), American Heart Association (AHA), North American Menopause Society (NAMS) and Canadian Task Force on Preventive Health Care recommend against use of HRT for the prevention of chronic diseases in postmenopausal women. <sup>(2)</sup>

Estrogen, however, is the most effective treatment available for relief of the menopausal symptoms that many women experience, including hot flashes, vaginal dryness, urinary symptoms and emotional lability. <sup>(3, 4)</sup>



## Hormone Replacement Therapy and Breast Cancer

With long-term oral use of postmenopausal estrogen replacement therapy ( ERT ) epidemiological and observational studies revealed an increase in breast cancer risk, relative risk ranging from 1.06 to 1.3 <sup>(5)</sup>. A re-analysis of original data from 51 epidemiologic studies comprising 52,705 women with, and 108,411 women without breast cancer found that for each year a woman used postmenopausal hormones, her risk of breast cancer increases by 2.3%. <sup>(6)</sup>

Various large cohort studies have shown that the addition of a progestogen in combined hormone replacement therapy (EPT) increases this risk further. Prospective randomized trials have confirmed this for the continuous combined regimen.<sup>(7)</sup> In the combined epidemiological analysis, treatment with estrogen plus progestin was associated with a higher risk of breast cancer than unopposed estrogen (relative risk 1.53 and 1.34



respectively) (6). This was also supported by the Million Women Study from the UK of over one million women ages 50 to 64 years.<sup>(8)</sup> Current use of HRT was associated with an increased risk of breast cancer (RR 1.30 and 2.0 for ERT and EPT respectively).

The Women's Health Initiative (WHI) was a set of clinical trials including two hormone trials (ERT and oral continuous combined EPT) in healthy postmenopausal women ages 50 to 79, which was scheduled to be completed in 2005. This trial was stopped prematurely because of an increased risk of breast cancer, CHD, stroke, and venous thromboembolism over an average follow-up of 5.2 years.

The WHI showed a significant increase in the risk of invasive breast cancer with continuous combined hormone replacement (HR 1.24). In contrast the WHI unopposed estrogen trial arm (which was stopped in early 2004 due to a slight increase in stroke risk) showed a slightly lower rate of breast cancer after an average follow-up of 6.8 years with unopposed estrogen when compared to placebo (HR 0.77).



### **Non-hormonal therapy for Hot flashes**

Faced with the above issues, what else can be offered to symptomatic women? Many nonhormonal agents have been assessed for their effectiveness in reducing menopausal hot flash symptoms. These include

#### **Non-Prescription Drugs (over the counter)**

- |                   |                          |
|-------------------|--------------------------|
| ❖ Black cohosh    | ❖ Evening primrose oil   |
| ❖ Melatonin       | ❖ Ginseng                |
| ❖ Dong quai       | ❖ Red clover Isoflavones |
| ❖ Soy isoflavones | ❖ Vitamin E              |
| ❖ Wild Yam        |                          |



#### **Prescription Medications**

- |               |   |
|---------------|---|
| ❖ Clonidine   | ❖ Fluoxetine  |
| ❖ Gabapentine | ❖ Mirtazapine   |
| ❖ Paroxetine  | ❖ Trazodone   |
| ❖ Venlafaxine | ❖ Belladonna/ergotamine tartrate/ Phenobarbital combination |

To our patients, some of these may be available and affordable...but the core issue is, are any of these effective? A confounding factor in most hot flash trials is the placebo response rate which has been reported to be between 18 and 40! <sup>(9)</sup>

In India we still have women considering menopause as something to be taken in their stride, and not too many are willing or able to take medication for a "natural event". In the USA, across oncology and gynecology clinics, most clinicians have found Venlafaxine (Effexor) to be the most useful nonhormonal treatment for hot flashes in practice. <sup>(10)</sup>

The summary of useful regimens for hot flashes with doses is listed below. These are mostly effective for short-term treatment. <sup>(9)</sup>

- ❖ Black Cohosh: 40 to 80 mg daily, from 8 weeks up to 1 year
- ❖ Clonidine: 0.1 mg daily, from 8 to 12 weeks
- ❖ Fluoxetine: 20 mg, 9 weeks
- ❖ Paroxetine: 20 to 40 mg, 4 weeks
- ❖ Soy and other isoflavones: 40 to 164 mg, 7 to 12 weeks
- ❖ Venlafaxine: 37.5 mg to 150 mg, 4 to 12 weeks

Black Cohosh (*Actaea / Cimicifuga racemosa*) is a popular over the counter herb, given as 40-80-mg/ day, whose exact mechanism of action is unknown, although it has been used in the USA for over 100 years. <sup>(11)</sup>

Soy isoflavones were observed to reduce vasomotor symptoms in Asian women who consume a soy rich diet. They contain phytoestrogens and can have estrogenic and antiestrogenic effects.

ACOG states that they may be useful for short-term treatment of vasomotor symptoms. However, due to possible estrogenic effects they should not be considered free of potential harm for women, particularly those who have an estrogen-dependent cancer.<sup>(9)</sup>

SSRIs and Venlafaxine: Selective Serotonin Reuptake Inhibitors like Fluoxetine (Prozac), Paroxetine (Paxil) and Venlafaxine (Effexor), a serotonin and norepinephrine reuptake inhibitor have shown an absolute risk reduction in hot flashes of 19 to 60% as compared to placebo, primarily in women with breast cancer. (9) The exact mechanism of action is unknown. It is better to start at low dosage and titrate to effect as transient adverse effects like insomnia, excitement, nausea, constipation and anorexia are reported.

Clonidine (Catapres) has been used orally, and as a patch, and probably reduces vascular reactivity hence helps alleviate hot flashes, by 15 to 20% as compared with placebo.<sup>(9)</sup>



### Treatment of Urogenital Symptoms

Women with symptoms of urogenital atrophy should be treated with vaginal moisturizers and lubricants. <sup>(12)</sup> If these are not effective use of low dose vaginal estrogen creams or vaginal estrogen ring is possible. This is controversial however, particularly in women with hormone-responsive breast cancer, as systemic absorption is known to occur with standard doses of vaginal estrogens. <sup>(13)</sup> Although it is suggested that lower doses may be safe and effective, more safety data is required.

### KEY POINTS FOR CLINICAL PRACTICE

- With increasing longevity women are spending more of their lives in the time period after cessation of periods, i.e. menopause
- There are many bodily changes just before, during and after menopause
- Replacement of hormones, estrogen and progesterone, has been considered
- The link between ovarian hormones and breast cancer raises concern for hormone therapy in all postmenopausal women
- Symptoms of menopause can be severe and affect the quality of life hence treatment of menopause needs to be a priority
- Short-term therapy for vasomotor symptoms includes Venlafaxine, other SSRIs or Clonidine, and non-prescription medications such as Soy Isoflavones or Black Cohosh
- Urogenital symptoms are first treated with vaginal lubricants, estrogen creams if used should be used in lowest effective dose for short time periods
- Bone health should be maintained preferably by standard non-hormonal therapies
- Quality of life and symptomatology need to be taken into account when choosing modality of treatment

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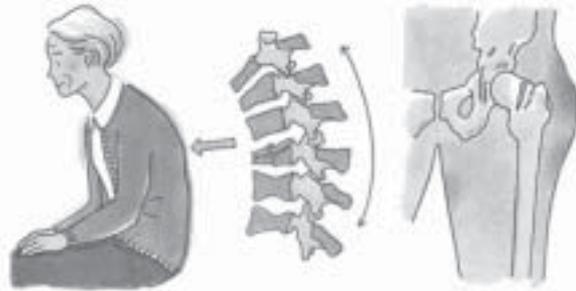
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## OSTEOPOROSIS

Dr. Reena J. Wani

### Introduction

Osteoporosis has often been called the "Silent Epidemic" as it is a disease that is becoming increasingly prevalent yet underdiagnosed and unmanaged till its consequences have already made their appearance. Hence as physicians, regardless of which speciality we belong to, we need to be aware of the underlying factors, clinical signs and sequelae of this disease. It has often been said, prevention is better than cure...here is one such situation where timely interventions have a major role in reducing later morbidity and mortality.



### Pathophysiology and Classification

Normally, bone formation and resorption are closely coupled. Osteoblasts (cells that make the organic matrix of bone and then mineralize bone) and osteoclasts (cells that resorb bone) are regulated by parathyroid hormone (PTH), calcitonin, estrogen, vitamin D, cytokines (eg, interleukin-1, tumor necrosis factor-alpha, granulocyte-macrophage colony-stimulating factor, interleukin-6), and other local factors such as prostaglandins.

Peak bone mass in men and women occurs by the mid 20s. Blacks reach higher bone mass than whites and Asians, while Hispanics have intermediate values. Men have higher bone mass than women. Bone mass plateaus for about 10 years, during which time bone formation approximately equals bone resorption. After this, bone loss occurs at a rate of about 0.3 to 0.5%/year. Beginning with menopause, bone loss accelerates in women to about 3 to 5%/year for about 5 to 7 years.

Dietary deficiency and inadequate exposure or reactivity to sunlight (due to lifestyle choices, cultural customs and/or aging) are identified as important risk factors for vitamin D inadequacy in Asian women. Non-uniform, epidemiological studies indicate a high prevalence of vitamin D inadequacy in postmenopausal women in Eastern Asia. Recommended remedial approaches are education campaigns and broad-based provision of vitamin D supplementation.<sup>(1)</sup>

Osteoporotic bone loss affects cortical and trabecular (cancellous) bone. Cortical thickness and the number and size of trabeculae decrease, resulting in increased porosity. Trabeculae may be disrupted or entirely absent.

Osteoporosis can develop as a primary disorder or secondarily due to some other factor.

### Primary osteoporosis

More than 95% of osteoporosis is primary; there are three types.

*Idiopathic osteoporosis* is uncommon but occurs in children and young adults of both sexes with normal gonadal function.

*Type I osteoporosis* (postmenopausal osteoporosis) results from increased osteoclast activity and affects primarily trabecular bone. It occurs between ages 51 and 75 and is 6 times more common in women than in men. Estrogen loss may elevate levels of cytokines, which are thought to increase recruitment and activity of osteoclasts in trabecular bone, resulting in increased bone resorption. Late menarche, early menopause, and nulliparity increase the risk. Although calcitonin levels are decreased in women compared with men, calcitonin deficiency does not appear to be important. In men, prematurely low levels of serum testosterone can increase osteoclast activity, causing type I osteoporosis. Type I is largely responsible for fractures affecting predominantly trabecular bone, such as vertebral compression fractures and Colles' (distal radius) fractures.

*Type II osteoporosis* (involutional or senile osteoporosis) results from the normal gradual decline in the number and activity of osteoblasts that occurs with aging and affects both trabecular and cortical bone. It typically affects patients > 60 and is twice as common in women as in men. In older women, types I and II often occur together. Estrogen deficiency is probably an important factor in both men and women, but reduction in Calcium or vitamin D intake or vitamin D synthesis or resistance to vitamin D activity-resulting in secondary hyperparathyroidism-may contribute. Vertebral compression fractures and fractures of the femoral neck, proximal humerus, proximal tibia, and pelvis can result.

Age-related bone loss in men is a poorly understood phenomenon, although increasing data on the pathophysiology of bone in men is becoming available. Most of what we know on bone pathophysiology derives from studies on women. The well-known association between menopause and osteoporosis is far from been disproven. However, male osteoporosis is a relatively new phenomenon. Its novelty is in part compensated for by the number of studies on female osteoporosis and bone pathophysiology. On the other hand, the deeper understanding of female osteoporosis could lead to an underestimation of this condition in the male counterpart. The longer life-span exposes a number of men to the risk of mild-to-severe hypogonadism which in turn we know to be one of the pathogenetic steps toward the loss of bone mineral content in men and in women. Hypogonadism might therefore be one among many corrigible risk factors such as cigarette smoking and alcohol abuse against which clinicians should act in order to prevent osteoporosis and its complications. Treatments with calcium plus vitamin D and bisphosphonates are widely used in men, when osteoporosis is documented and hypogonadism has been excluded. The poor knowledge on male osteoporosis accounts for the lack of well shared protocols for the clinical management of the disease.<sup>(2)</sup>

### **Secondary osteoporosis**

Secondary osteoporosis accounts for < 5% of osteoporosis cases. The causes (see Table 1: Osteoporosis: Causes of Secondary Osteoporosis) may also aggravate bone loss and increase fracture risk in patients with primary osteoporosis.

Table 1
<b>Causes of Secondary Osteoporosis</b>
Chronic renal failure
COPD
Drugs (eg, corticosteroids, ethanol, phenytoin, tobacco, barbiturates, heparin)
Endocrine disease (eg, glucocorticoid excess, hyperparathyroidism, hyperthyroidism, hypogonadism, hyperprolactinemia, diabetes mellitus)
Hypervitaminosis A
Immobilization
Liver disease
Malabsorption syndromes
Malignancy
Prolonged weightlessness (as found in space flight)
Rheumatoid Arthritis
Sarcoidosis

### **Risk Factors**

Because stress, including weight bearing, is necessary for bone growth, immobilization or extended sedentary periods result in bone loss. Being thin predisposes to decreased bone mass. In fact it has been observed that obese menopausal women are less prone to osteoporotic fractures due to higher endogenous estrogen production from peripheral fat stores, and more padding which lessens the chance of fracture when they fall!! Insufficient dietary intake of Calcium, Phosphorous, and vitamin D predisposes to bone loss, as does endogenous acidosis (eg, high-protein diets). Cigarette smoking and excessive caffeine or alcohol use also adversely affect bone mass. Whites and Asians are at higher risk. A family history of osteoporosis also increases risk. Other risk factors (eg, decreasing amounts of sex hormones) predispose to specific types of osteoporosis.

### **Symptoms and Signs**

Most of the chronic pain typical of osteoporosis results from fractures, which may develop after minimal, inapparent, or no trauma. Patients may be asymptomatic for years, until fractures begin to occur. Eventually, patients often develop pain in the bones or muscles, particularly of the back. Vertebral compression fractures are common, usually in weight-bearing vertebrae (T6 and below). The pain begins acutely, usually does not radiate, is aggravated by weight bearing, may produce

local tenderness, and generally begins to subside in 1 week. However, residual pain may last for months or be constant.

Multiple thoracic compression fractures eventually cause dorsal kyphosis, with exaggerated cervical lordosis (dowager's hump). Abnormal stress on the spinal muscles and ligaments may cause chronic, dull, aching pain, particularly in the lower back. Fractures can develop at other sites, commonly the hip or wrist, usually from falls.



### Screening and Diagnosis

Dual-energy x-ray absorptiometry (DEXA) screening is recommended for all women over 65 years of age. Bone density should also be measured in women between 50 and 65 who have risk factors, including a family history of osteoporosis, a history of fragility fractures, and low body weight. Screening is also recommended for both men and women who have had fragility fractures, even at younger ages.

Osteoporosis should be suspected in patients who sustain fractures after only mild or trivial trauma; older adults, particularly those with risk factors and unexplained back pain; patients with decreased bone density that is incidentally noted on radiographic studies; and patients at risk of secondary osteoporosis. If radiographic studies have been obtained or are necessary to evaluate symptoms (e.g. back pain) osteoporosis may be obvious. However, radiographic studies are often equivocal, and the diagnosis should be established by DEXA.

### Plain x-rays

Bones show decreased radiodensity and loss of trabecular structure, but not until about 30% of bone has been lost. A loss of horizontally oriented trabeculae increases the prominence of the cortical end plates and of vertically oriented, weight-bearing trabeculae. Loss of height and increased biconcavity characterize vertebral compression fractures. Thoracic vertebral fractures may produce anterior wedging. In long bones, although the cortices may be thin, the periosteal surface remains smooth. Vertebral fractures at T4 or above suggest malignancy rather than osteoporosis.

### DEXA scanning

In addition to its use in screening, DEXA is diagnostic for osteoporosis, predicts the risk of fracture, and can be used to follow treatment response. Bone density of the lumbar spine, hip, distal radius or ulna, or the entire body can be measured. (Quantitative CT scanning can produce similar measurements in the spine or hip.) Measurement at the spine may show osteoporosis earlier than at the hip, but the hip is a better indicator in elderly patients because osteoarthritis of the spine may mask the presence of osteoporosis. A DEXA result of  $> 1$  standard deviation from the average value in 25-yr-old sex- and race-matched controls is defined as osteopenia and suggests an increased risk for osteoporosis;  $> -2.5$  is diagnostic for osteoporosis.

**WHO criteria for the diagnosis of Osteoporosis:**

Based on the BMD as measured by DEXA expressed as T score.

Normal : BMD within -1 SD

Osteopenia : BMD within -1.0 and -2.5 SD

Osteoporosis : BMD less than -2.5 SD

Severe Osteoporosis - osteoporosis as defined above with one or more fragility fractures

***Other testing***

Once osteoporosis is diagnosed, patients should be checked for causes of secondary osteoporosis. Serum Calcium should be measured to rule out asymptomatic hyperparathyroidism. PTH levels may be increased in type II patients with decreased Calcium absorption or hypercalciuria. Other tests such as thyroid-stimulating hormone or free thyroxine to check for hyperthyroidism, vitamin D levels, measurements of urinary free cortisol, and blood counts and other tests to rule out malignancy, especially myeloma (eg, serum protein electrophoresis), should be considered depending on the clinical presentation. Serum alkaline phosphatase is usually normal but may be elevated by recent fracture.



Patients with weight loss should be screened for GI disorders as well as malignancy. Bone biopsy is reserved for unusual cases (eg, young patients with pathologic fractures and no apparent cause). Levels of serum or urine N-telopeptide crosslinks (NTX) or free deoxypyridinoline (DPYR) may reflect increased breakdown of collagen. These tests are not sufficiently accurate for routine clinical use but may be used to assess the effectiveness of therapy.

**Osteopenia: Differentiating Osteoporosis and Osteomalacia**

Osteopenia is decreased bone mass. Two metabolic bone diseases decrease bone mass: osteoporosis and osteomalacia. In osteoporosis, there is a decrease in bone mass with a normal ratio of bone mineral to bone matrix. In osteomalacia, the ratio of bone mineral to bone matrix is low.

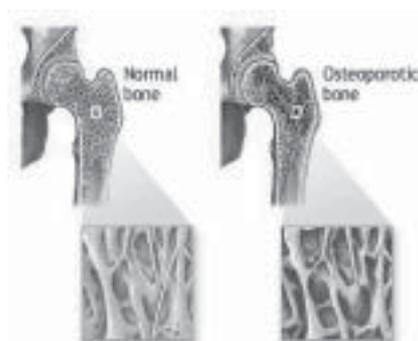
Osteoporosis results from a combination of low peak bone mass, increased bone resorption, and impaired bone formation. Osteomalacia is due to impaired mineralization, usually because of severe vitamin D deficiency or abnormal vitamin D metabolism. Osteoporosis is much more common than osteomalacia in the US. The two disorders may coexist, and their clinical expression is similar; moreover, mild to moderate vitamin D deficiency can occur in osteoporosis.

**Prevention and Treatment**

The goals are to preserve bone mass, prevent fractures, decrease pain, and maintain function. Treatment and preventive measures are appropriate for patients with documented osteoporosis,

patients taking long-term systemic corticosteroids, and patients at high risk (eg, osteopenia with multiple risk factors).

Osteoporosis affects one in three women. There has been some confusion among women and health professionals about the management of osteoporosis since the publication of the Women's Health Initiative and Million Women studies. This guidance regarding estrogen-based and non-estrogen-based treatments for osteoporosis responds to the controversies about the benefits and risks of individual agents. Treatment choice should be based on up-to-date evidence and targeted to individual women's needs.<sup>(3)</sup>



### Isoflavones in Osteoporosis

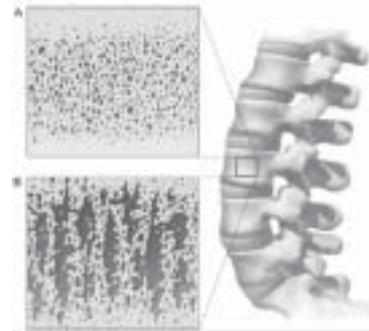
Soy isoflavones are natural products that could be used as an alternative to menopausal hormone therapy because they are structurally and functionally related to 17beta-estradiol. In vitro and animal studies have shown that they act in multiple ways to exert their bone-supporting effects. They act on both osteoblasts and osteoclasts through genomic and nongenomic pathways. Epidemiological studies and clinical trials suggest that soy isoflavones have beneficial effects on bone mineral density, bone turnover markers, and bone mechanical strength in postmenopausal women. However, there are conflicting results related to differences in study design, estrogen status of the body, metabolism of isoflavones among individuals, and other dietary factors. A review article designed to address the effects of soy isoflavones on bone metabolism in postmenopausal women and their place in the prevention and treatment of postmenopausal osteoporosis suggests that the long-term safety of soy isoflavone supplements remains to be demonstrated.<sup>(4)</sup>

The effects of isoflavones on bone loss appear inconsistent in randomized controlled trials. Therefore, a group of investigators used a statistical method of combining these diverse data to clarify the effects of soy isoflavone intake on spine bone loss. Ten studies with a total of 608 subjects were selected for meta-analysis. The spine bone mineral density in subjects who consumed isoflavones increased significantly by 20.6 mg/cm<sup>2</sup> (95% confidence interval: 4.5-36.6 mg/cm<sup>2</sup>) in comparison to that in subjects who did not consume isoflavones. Isoflavone intake vs placebo intake increased spine bone mineral content by 0.93 g (95% confidence interval: -0.37 to 2.24 g) with borderline significance. They concluded that isoflavone intervention significantly attenuates bone loss of the spine in menopausal women. These favorable effects become more significant when more than 90 mg/day of isoflavones are consumed and soy isoflavone consumption for 6 months can be enough to exert beneficial effects on bone in menopausal women.<sup>(5)</sup>

Like other over the counter products, there is much variation in doses and schedules used with isoflavones which may explain the lack of clear-cut guidelines and demonstration of clinical efficacy. However for women with symptoms of menopause and osteoporosis who are unable or unwilling to take hormones, they may be a useful option.<sup>(6)</sup>

### **Bisphosphonates in Osteoporosis**

Biphosphonates have been used for Paget's disease of the bone, treatment and prevention of glucocorticoid-induced osteoporosis, in postmenopausal women and for treatment of osteoporosis in men.



Commonly used agents are<sup>(7, 8)</sup>

Alendronate : daily dosing of 5-10 mg or once a week dosing of 35 to 70 mg

Etidronate : less effective than alendronate in increasing BMD

Risedronate : 1 mg daily or 35 mg once a week

Ibandronic acid : Newer agent with monthly dosing of 150 mg

- It offers the option of reduced dosing, improving compliance with good efficacy
- Clinical outcome is increasing BMD and reducing vertebral fractures

#### **Advantages of bisphosphonates:**

- They are the most thoroughly investigated agents we have for the treatment of osteoporosis and the prevention of fractures in postmenopausal osteoporosis.
- They prevent osteoclastic bone resorption, and reduce fracture risk within 12-18 months of treatment initiation.
- Given the cost, ease of once-weekly dosing, and minimal side-effects, a bisphosphonate is the agent of choice for bone health unless the woman has symptoms necessitating estrogen use

#### **Mechanism of Action**

- Act by inhibiting bone resorption via actions on osteoclasts or on osteoclast precursors; decreases the rate of bone resorption, leading to an indirect increase in bone mineral density.
- In Paget's disease, characterized by disordered resorption and formation of bone, inhibition of resorption leads to an indirect decrease in bone formation; but the newly-formed bone has a more normal architecture.
- They prevent osteoclastic bone resorption, and reduce fracture risk within 12-18 months of treatment initiation.

#### **Mode of use**

- Oral bisphosphonates must be taken on an empty stomach with a full glass of water, and the patient must remain upright for approximately more than 30 min. Weekly therapy is generally preferred for its greater convenience and probably fewer adverse effects
- If a patient cannot tolerate oral bisphosphonates, pamidronate or zoledronic acid can be given by IV infusion. These are often used in breast cancer patients(see other section) However, these have not yet been shown to prevent fractures

### Disadvantages of Biphosphonates

- 1. Poor oral absorption
- 2. Side-effects are mainly gastrointestinal, with esophageal irritation hence must be given with a large volume of water, and care taken to avoid recumbency after dosing. Half an hour later patient should eat something.
- 3. Gastrointestinal mucosa irritation: Esophagitis, esophageal ulcers, esophageal erosions, and esophageal stricture (rare) have been reported with oral bisphosphonates; risk increases in patients unable to comply with dosing instructions. Use with caution in patients with dysphagia, esophageal disease, gastritis, duodenitis, or ulcers (may worsen underlying condition).
- 4. Bone/joint/muscle pain: Infrequently, severe (and occasionally debilitating) bone, joint, and/or muscle pain have been reported during bisphosphonate treatment. The onset of pain ranged from a single day to several months. Symptoms usually resolve upon discontinuation. Some patients experienced recurrence when rechallenged with same drug or another bisphosphonate; avoid use in patients with a history of these symptoms in association with bisphosphonate therapy.
- 5. Hot flashes may not be benefited
- 6. Rare cases of jaw necrosis described with Alendronate and other biphosphonates

### Other Options <sup>(9)</sup>

- Salmon calcitonin is less effective than bisphosphonates for treating osteoporosis. The subcutaneous dose is 100 IU/day or every other day; the nasal spray dose is 200 U/day in alternating nostrils (one spray). Salmon calcitonin may provide short-term analgesia after an acute fracture.
- Parathyroid hormone, which stimulates new bone formation, is generally reserved for patients who fail to respond to antiresorptive drugs, as well as Calcium, vitamin D, and exercise. Teriparatide: a form of human parathyroid hormone, is given daily as an injection, for up to 24 months. It increases bone density and reduces the risk of spine and other fractures. When given daily by injection for an average of 20 months, synthetic parathyroid hormone (PTH 1-34; teriparatide) increased bone mass and reduced fractures.
- Raloxifene is a selective estrogen receptor modulator (SERM) that may be appropriate for prevention and treatment of osteoporosis in women who cannot take bisphosphonates. It reduces vertebral fractures by about 50% but has not been shown to reduce nonvertebral fractures

### Hormones and Osteoporosis

The clinical aftermath of the reporting of the initial findings of the Women's Health Initiative (WHI) in 2002 was a profound reduction in the use of hormone therapies by menopausal women. This reduction led to a well-documented increase in vasomotor symptoms and vaginal atrophy among those women who discontinued their hormone regimens. However, another adverse impact

among these women, as well as many other menopausal women, is the well recognized increased likelihood of osteoporosis resulting from the decline in circulating estradiol levels associated with natural and surgical menopause. Although the use of non-hormonal drugs such as bisphosphonates has been shown to reduce the risk of fracture in women with osteoporosis, bisphosphonates have not been shown to reduce the risk of fracture in non-osteoporotic women. Indeed, only oral estrogen (as demonstrated in the WHI studies) has been shown to reduce the risk of fracture in osteoporotic and non-osteoporotic women. As non-oral hormone therapies (as discussed in other section) have been shown to be as effective in treating vasomotor symptoms and vulvovaginal atrophy and to have a different (and perhaps more beneficial) physiological effect than oral regimens, we need to assess the impact of non-oral hormone regimens on bone mineral density and fracture risk. Although there are no clinical trials that primarily assess the impact of non-oral regimens on fracture risk in menopausal women, numerous studies are consistent in demonstrating the positive impact of non-oral regimens in maintaining and increasing bone mineral density among users, even for those women using estrogen doses that are considered to be "too low" to have a beneficial impact on other menopausal symptoms.<sup>(10)</sup>

In another narrative review of the current literature, the traditional risk factors and patient profiles leading to cardiovascular disease and osteoporosis were examined. They discussed the interrelationships between risk factors and common pathophysiological mechanisms for cardiovascular disease and osteoporosis and evaluated the increasing evidence that supports an association between these disabling conditions. The study revealed that vascular health appears to have a strong effect on skeletal health, and vice versa and highlighted the importance of addressing the risk benefit of preventive interventions in both conditions. They discussed how both sexes are affected by these chronic conditions and the importance of considering the unique risk of the individual and showed that habitual physical activity is an effective primary and secondary preventive strategy for both cardiovascular disease and osteoporosis.<sup>(11)</sup>

To provide an overview of current research regarding hormone replacement therapy and to assist healthcare providers to better educate patients about potential benefits of this therapy, a systematic review of healthcare literature was conducted with 602 articles selected from CINAHL, Medscape, Pubmed, and Medline databases. Keywords directing the search included hormone replacement therapy, benefits of hormone replacement therapy and trends, hormone replacement therapy and osteoporosis, hormone replacement, and menopause symptoms. According to the literature, HRT can assist women with postmenopausal symptoms. In addition, research shows that HRT can help some postmenopausal women with selected comorbid conditions such as osteoporosis, type II diabetes, certain cardiovascular pathologies, and colorectal cancer. The decision as to who should use any form of HRT needs to be based on the individual woman's needs, quality of life, and potential risks versus benefits. The researchers concluded that HRT has been a benefit to many women in the treatment of postmenopausal symptoms. Recent studies have shown that HRT, whether it is combined estrogen and progestin therapy, or estrogen-only therapy, can help postmenopausal women with osteoporosis and some selected comorbid conditions. Recent research indicates that some women are dying from comorbid conditions rather than breast cancer. Although the research regarding HRT in some areas may be limited, further research adds to existing

knowledge and offers new ideas and possibilities in the treatment of postmenopausal symptoms and selected comorbid conditions. Certainly HRT can improve quality of life and possibly longevity for selected women. Ongoing research is needed to further validate such benefits, as well as to further explore the risks and benefits of long-term HRT. Increased knowledge about HRT will help healthcare providers better educate patients about the potential benefits of HRT, while providing documentation about who should take selected types of HRT or whether alternative treatment is preferred. <sup>(12)</sup>

### ***Current Advice for HRT Use***

- HRT should be used for treatment of specific signs and symptoms and low bone density
  - HRT has no place in secondary prevention of CVD, but may be indicated for early menopausal women
  - HRT started in older women, 60-79 may do early harm, with increased heart attacks, strokes and vascular dementia before any benefit is obtained
  - Dose, route depends on age and signs and symptoms, for vasomotor signs and symptoms, use oral or transdermal estrogen with cyclical progesterone (14d)
  - Lowest effective dose
  - Review indication, need for HRT annually
  - 5 year duration of treatment
  - Annual mammogram, 6 monthly breast examination
- It does appear that HRT, especially Estrogen is not only safe, but also beneficial in younger women (45-60)

### **SUMMARY :**

#### ***Osteoporosis Prevention***

Non-Prescription Drugs (over the counter)<sup>(6,9)</sup>

- All men and women should consume at least 1000 mg of elemental Calcium daily
- 1200 to 1500 mg/day is recommended for postmenopausal women
- Vitamin D in doses of 400 U once/day is generally used
- Up to 1000 U/day of Vitamin D is safe
- Currently, the case-finding approach is best, as antiresorptive drugs given to women with or without fractures reduce the risk of fracture by about 50%. Women at high risk for fractures, or those with prior fracture should be treated.<sup>(13, 14)</sup>

#### **Osteoporosis:Treatment Goals**

##### **Preserving bone mass**

-The rate of bone loss can be slowed with drugs

-Calcium and vitamin D intake and physical activity must be adequate for drug treatment to be effective

-Risk factor modification can include maintaining adequate body weight, increasing weight-bearing exercise, minimizing caffeine and alcohol intake, and stopping smoking

-The optimal amount of weight-bearing exercise is not established, but an average of 30 min/day is needed

#### Medications

- Bisphosphonates are first-line drug therapy. By inhibiting bone resorption, bisphosphonates preserve bone mass and can decrease vertebral and hip fractures by 50%. To treat osteoporosis, alendronate can be given at doses of 10 mg orally once/day or 70 mg orally once/week or risedronate at 5 mg orally once/day or 35 mg once/week
- Isoflavones may be an acceptable non-prescription alternative

#### *Decrease pain*

-Acute back pain from a vertebral compression fracture should be treated with orthopedic support, analgesics, and (when muscle spasm is prominent) heat and massage

-Chronic backache may be relieved by an orthopedic garment and exercises to strengthen paravertebral muscles.

#### *Maintain function*

-Encourage patients to be active

#### *Preventing fractures*

-Many elderly patients are at risk for falls because of poor coordination, poor vision, muscle weakness, confusion, and use of drugs that cause postural hypotension or alter the sensorium

-Educating patients about risks of falls and fractures

-Developing individualized programs to increase physical stability and attenuate risk can help

- Strengthening exercises may increase stability

-Hip pads can prevent injury despite falls

### **ROLE OF DOCTOR**

Counsel the patient

Carefully rule out contraindications for HRT

Consider the options

Calcium, Vit D, Biphosphonates useful

Choice is finally to be made by the person taking the medications!!



### KEY POINTS FOR CLINICAL PRACTICE

- Osteoporosis is a progressive metabolic bone disease that decreases bone density (bone mass per unit volume), with deterioration of bone structure.
- Skeletal weakness leads to fractures with minor or inapparent trauma, particularly in the thoracic and lumbar spine, wrist, and hip. Acute or chronic back pain is common.
- Diagnosis is by dual-energy x-ray absorptiometry.
- Prevention and treatment involve Ca and vitamin D supplements, exercises to maximize bone and muscle strength and minimize the risk of falls, and drug therapy to preserve bone mass or stimulate new bone formation.
- Post menopausal patients form a large and significant group who may benefit from specific therapy
- Biphosphonates are the first line of treatment for post-menopausal women with osteoporosis and no other menopause problems
- Women on HRT for symptoms of menopause are protected by the hormones from osteoporosis
- Significant reduction in morbidity and mortality can be achieved by focusing on appropriate measures for this "silent epidemic".

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#### **Websites for Osteoporosis-related Information**

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2. <http://www.emedicine.com>
3. <http://en.wikipedia.org>
4. <http://www.kneereplacement.com>
5. <http://www.mayoclinic.com>
6. [www.menopause.org](http://www.menopause.org)
7. [www.nlm.nih.gov/medlineplus](http://www.nlm.nih.gov/medlineplus)
8. [www.womenhealthfocus.com](http://www.womenhealthfocus.com)
9. [www.medicinenet.com](http://www.medicinenet.com)
10. [www.clevelandclinic.org](http://www.clevelandclinic.org)

## MENOPAUSE MANAGEMENT AFTER BREAST CANCER

Dr. Reena J. Wani

### Clinical Scenario

Mrs ABC, 48 years old came to me with complaints of hot flashes. She was perimenopausal, and had recently been diagnosed to have metastatic breast cancer for which bilateral oophorectomy was done, and she was started on tamoxifen therapy, being ER positive.

### Several issues needed to be addressed in her care

- ❖ What is the relationship of hormones and breast cancer?
- ❖ What are the available options?
- ❖ Will the chosen treatment have any effect on her cancer and survivorship?
- ❖ How long should treatment be continued?
- ❖ What about quality of life issues?

What is the standard of care today?

### Breast Cancer: Current Therapy and Follow-up

Early stage breast cancer (i.e. Stage I or II) can be treated effectively by mastectomy, or by excision of the tumor mass followed by radiation to the residual ipsilateral breast (breast conservation therapy, BCT). This results in equivalent cancer-specific survival compared to mastectomy and affords a cosmetic advantage by preserving the breast. However BCT requires more health care resources and infrastructure than mastectomy. Estrogen receptor testing allows patient selection for hormonal treatment such as tamoxifen, oophorectomy, and aromatase inhibitors). Chemotherapy is needed to treat node-positive, locally advanced breast cancers, which represent the most common clinical presentation of disease in low-resource countries. When chemotherapy is not available, patients with locally advanced, hormone receptor- negative cancers can only receive palliative therapy. <sup>(1)</sup>

### Need to Treat Breast Cancer Survivors

Symptoms of menopause in breast cancer survivors can result from

- ❖ Direct effect of cancer treatment such as oophorectomy, ovarian suppression, chemotherapy-induced ovarian failure and anti-estrogens
- ❖ As a spontaneous event
- ❖ After discontinuation of hormone replacement therapy



The onset of menopausal symptoms in these women should not be ignored, as it can have a long-lasting effect on body image, sexual function, self-esteem and overall quality of life. As the incidence of breast cancer increases, and survival continues to improve, the number of women needing help for menopausal symptoms will probably rise, and safe and effective therapies are urgently needed.<sup>(2)</sup>

### **Estrogen to treat menopausal symptoms in Breast Cancer Survivors**

As discussed earlier, hormone therapy that contains estrogen is the most effective treatment for menopausal symptoms in healthy women<sup>(2, 3)</sup>. However, the close association of hormones and genesis of breast cancer has been a cause of concern, that dormant micrometastases may be stimulated to grow in breast cancer survivors. Even though available epidemiological evidence suggests that the magnitude of risk conferred by ERT in women with and without a family history of breast cancer is similar, some groups (for example the American College of Physicians) do not recommend ERT even in these women.<sup>(4)</sup>

A personal history of breast cancer has traditionally been considered a contraindication to the use of ERT. However most observational studies have reported no increase in the risk of recurrence with estrogen therapy<sup>(4,5,6)</sup>. Clinical trial data are conflicting, and suggest that estrogen therapy may be associated with excessive risk. In the HABITS trial of 434 women with breast cancer, after a median follow-up of 2.1 years, 26 women in the hormone group and seven in the non-hormone group had a breast cancer event (Relative hazard RH 3.5). Based upon the excessive risk in the hormone group, the study was terminated in December 2003.<sup>(7)</sup> Some clinicians have used ERT for women with low-risk breast cancer such as small tumors, negative lymph nodal status, long disease free survival, or estrogen receptor negative tumors who have received adequate treatment and have menopausal symptoms<sup>(4)</sup>. Others suggest that the prevalent opinion that estrogens and estrogen treatment are deleterious for breast cancer needs to be revisited.<sup>(6)</sup>

To summarize, there are many problems facing the clinician dealing with menopausal symptoms after breast cancer- not only is there lack of consistency and lack of biological plausibility from the plethora of studies quoted, there is also a lack of relevance of some of the randomized clinical data to daily practice work.<sup>(8)</sup> Certain groups on the other hand have gone on record to say that the risk of breast cancer associated with HRT use has been underestimated, and that HRT is no longer an acceptable form of treatment for most women.<sup>(9)</sup>

### **Bone Health in Breast Cancer Survivors**

The adjuvant systemic treatments for breast cancer often have adverse effects on bone metabolism, with increased bone loss which may result in osteoporosis and associated fractures. These effects are not only due to direct effect of chemotherapy, but also endocrine-related: induction of an early menopause by chemotherapy and ovarian ablation, or further suppression of postmenopausal circulating estrogens by aromatase inhibitors.<sup>(10)</sup> Hence strategies to prevent osteoporosis are necessary. Risk factors for osteopenia should be assessed, and these women should be on adequate doses of calcium, and Vitamin D. Regular exercise and smoking cessation, if needed, should be emphasized. A biphosphonate such as etidronate or pamidronate is usually preferred to estrogen therapy in these women.<sup>(4)</sup>

## Osteoporosis and Breast Cancer

Third-generation aromatase inhibitors (AIs) are replacing tamoxifen as adjuvant therapy in postmenopausal women with hormone-sensitive breast cancer due to their superiority shown in several recent head-to-head trials. Healthy postmenopausal women normally experience age-related side effects, and in postmenopausal women with breast cancer, these symptoms may be exacerbated by adjuvant endocrine therapy. The AIs -- anastrozole, exemestane, and letrozole -- are generally well tolerated: most adverse events are mild to moderate and common to menopause. Common short-term AI-associated toxicities are hot flushes, musculoskeletal complaints/arthralgia, and bone loss, all of which can be effectively managed. AIs may lack the cardioprotective and lipid-lowering effects of tamoxifen but, in contrast to tamoxifen, do not increase the risk of serious life-threatening thromboembolic or cerebrovascular events or endometrial cancer. A review evaluated the current literature regarding bone health, lipid metabolism, cardiovascular disease, gynecologic health, and cognition in postmenopausal women receiving adjuvant AI therapy. They concluded that every patient should be individually assessed with respect to therapy risks and benefits. Lifestyle, comorbidities, and concomitant medications must be considered, and the importance of compliance to adjuvant therapy should be discussed before selecting a treatment regimen. The superior efficacy of adjuvant AI therapy will in most cases outweigh the risk of bothersome side effects that can be prevented or easily managed. <sup>(11)</sup>

Recently, concerns of bisphosphonate-induced renal safety and osteonecrosis of the jaw have emerged. Studies evaluating bisphosphonates in women with breast cancer have reported lower rates of renal dysfunction than those reported in patients with metastatic cancer receiving bisphosphonates, and no cases of jaw osteonecrosis. The use of bisphosphonates in this population requires further study to more clearly define the most appropriate timing and length of therapy as well as the long-term efficacy and safety of these drugs. Until these data become available, balancing the safety concerns with the potential benefits of I.V. bisphosphonates to minimize or prevent AI-induced bone loss in women with early-stage breast cancer is required. <sup>(12)</sup>

### Summary

Patients of breast cancer are a special group who may have severe symptoms of menopause. Principles of menopause management in general of course should be applied, but dealing with severe hot flushes with standard non-hormonal therapies is a preferred option. Bisphosphonates seem to be the treatment of choice for osteoporosis in these women. Quality of life and symptomatology need to be taken into account. Properly chosen treatments should not adversely affect their survival.

With increased survivorship and complex issues of clinical management of menopausal symptoms in this special group, special consideration and individualized strategies are required.

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**PATIENT INFORMATION :****MENOPAUSE- All you wanted to know but didn't know whom to ask!!**

These are frequently asked questions by persons around the world, and should help us to clarify menopause related questions for our women. The answers are in simple terms.

*Q. What is menopause?*

The latin word 'menopause' means 'the ending of menstruation'. It is the time period during which the monthly menstrual cycle ceases and the female sex hormones diminish rapidly to almost none at all.

*Q. Are the symptoms of menopause more common today?*

Every woman faces menopause. Some have it easily, while some have serious problems associated with it. Fifty years ago, when one would live for merely 62 years, 12 years of estrogen deficiency-associated with menopause was not that relevant. Now that most women live into their 80's there is a period of over 30 years for the effect on body systems to become apparent

*Q. Does menopause occur only with age?*

Menopause occurs when the ovaries cease to secrete the sex-hormones (estrogen and progesterone). Usually it occurs as one grows older and ovaries mature. However, in certain other situations like cancer-chemotherapy, radiation therapy or operative surgery on the ovaries (or rarely, pre-maturely) the ovaries stop functioning and/or are removed leading to the symptoms of menopause. Other operations to remove uterus and the removal of uterus with ovaries (Hysterectomy) will also lead to stoppage of periods.

*Q. What are hot flushes?*

Hot flushes are one of the commonest complaints. They are characteristically described as a sudden sensation of heat radiation and reddening of skin mainly confined to head and neck, lasting for a few seconds to minutes. It is usually followed by excessive perspiration.

*Q. What are the urinary symptoms associated with menopause?*

Urinary system gets commonly affected due to changes of menopause. Women may complain of increased frequency, urgency, painful urination (dysuria) and loss of urine on straining (stress incontinence).

*Q. Are any other complaints commonly seen in India in the time before menopause?*

The pattern of menopausal symptoms experienced by Asian women appears to be different when compared to their western counterparts. Asian women predominantly complained of backache, muscle pain, shoulder pain or joint pain but suffered less frequently from vasomotor disturbances.

*Q. How does menopause affect sexual desire?*

Many women remain sexually active throughout their post menopausal years. In general, sexual desire (sex drive) decreases with age in both sexes, but each individual is different. Although some experience a significant decline in desire, a few have increased interest, and others notice no change at all.

*Q. Is weight gain related to menopause?*

Midlife weight gain appears to be mostly related to aging and lifestyle, but menopause also contributes to the problem. Factors like changed food habits, sedentary lifestyles are more important than metabolic changes.

Menopause is associated with increased fat in abdominal region. Behavioral factors, particularly decreased exercise and increased alcohol and food consumption, are more closely linked to weight gain than menopause. With aging, muscle mass often decreases, while fat often increases. Body shape typically changes from a "pear" (wide hips and thighs) to an apple (wide waist).

*Q. As menopause is a natural event, why should I take treatment ?*

Though menopause is a natural event, in order to reduce distressing symptoms of it and to prevent osteoporosis and other chronic illnesses, treatment is necessary. There are many other conditions like pregnancy which are natural...still we do treat them - thus why not treat menopause??

*Q. Will the treatment help me to stay young?*

Treatment relieves distressing symptoms of menopause and improves sense of wellbeing and can restore sexual life. However medical therapy alone is not an "elixir of youth" and lifestyle changes are beneficial to maintain your health.

*Q. What medical treatment is available for symptoms of menopause?*

Depending on the indication there are many options. Your doctor can help you decide which is most suitable for you. There are many medications, including

- Hormone replacement therapy HRT ( estrogen with/without progesterone)
- Local estrogen containing creams for urogenital symptoms
- Bisphosphonates, SERMS (selective estrogen receptor modulators), salmon calcitonin for bone health
- Isoflavones which mimic the action of estrogen
- Clonidine, Fluoxetine, Venlafaxine for hot flashes
- Other over the counter products for hot flashes

*Q. Who should not take hormones?*

Any hormonal medicine should be started in consultation with your doctor. Women who are unsuitable for hormones include those women having undiagnosed vaginal bleeding, cancer of breast and endometrium, history of venous thromboembolism, active liver disease and those who are unwilling/ unable to follow-up

*Q. What are the risks of cancers with hormones?*

There is always a fear that hormones may cause cancer. In well-selected cases, use of hormones for different indications is very safe...in fact that is why the oral contraceptive pill is so popular!

Use of hormones in women has been studied and the following general findings are

- no increased risk of- squamous cell carcinoma, adenocarcinoma of endometrium, colorectal cancers
- probably no increased risk of -ovarian cancer , adenocarcinoma of cervix , cancer of breast, after 2 years of stopping hormones
- increased risk of- endometrial cancer and breast cancer after 5 years of use

*Q. Are there any benefits of taking hormones?*

Estrogen, with or without progesterone is a natural hormone which "replaces" or puts back what the ovary was producing before menopause occurred. These hormones prevent osteoporosis, urogenital atrophy, skin changes and may reduce atherosclerosis and cardiovascular diseases if started in the early postmenopausal period.

*Q. By what are different routes can hormones (HRT) can be given?*

Oral (by mouth)

Transdermal (as a skin patch or gel to be applied)

Intravaginal rings (to be inserted into the vagina)

*Q. What tests should be done and when to assess my health?*

All women will benefit from regular health check-ups, but more so in the later years of life, around menopause when certain tests are recommended. These include

- annual screening for gynecological problems
  - mammogram
  - pelvic examination
  - cervical cytology ( Pap smear)
- six monthly breast examination
  - You can learn how to do a regular breast self-examination on yourself.
- Screening tests for osteoporosis may be required such as ultrasound screening, DEXA scan or computerized tomography which can suggest if your bones are weak and you are at risk of fractures.

*Q. Who should start HRT ? Do all women need to take hormones?*

Various studies and world authorities have said that women who have moderate/ severe symptoms of menopause, or documented osteoporosis/ fragility fractures will benefit from hormones. All women however need not take hormones.

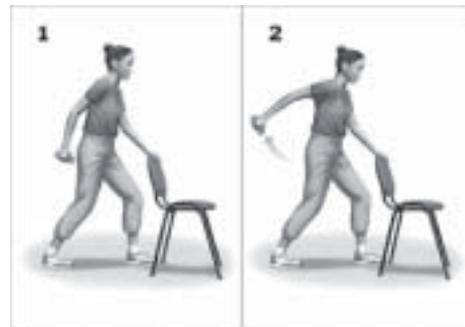
*Q. What lifestyle changes are advised for menopausal women?*

Being healthy and feeling young and fit is something which cannot happen overnight, nor will it happen by swallowing medications only! You need to adopt healthy habits from your youth such as

- Some form of aerobic exercises, like brisk walking
- To maintain bone health include weight bearing exercise, resistance or weight training

under suitable guidance

- Optimal calcium intake in diet by a balanced diet with calcium rich foods
- Avoid/give up smoking and alcohol as both of these are usually implicated in many chronic diseases, cancer and osteoporosis



*Q. Are there any alternatives available for HRT?*

There are many described in studies and literature, such as life style measures, local therapy, pharmacological alternatives like isoflavones, complementary interventions like acupuncture, reflexology, diet supplements and homeopathy. However the effectiveness of each method is different and results vary depending on dose and patient characteristics.

*Q. What short term treatments are available for hot flushes?*

Many treatments are described, like SSRI (Selective Serotonin re-uptake inhibitors) such as fluoxetine, SNRI (Selective Noradrenaline re-uptake inhibitors )like venlafaxine, soya & other isoflavones , and other alternative therapies like acupressure, reflexology and alternative medicines (homeopathy and ayurvedic medicines). Results and dosages are variable.

However it is seen that the most effective treatment for hot flashes in most women is estrogen replacement therapy.

*Q. Which medications are available over the counter?*

Certain medications used for menopause management are available without a prescription, however it is advisable to start them in consultation with a doctor. These medications may be having some placebo effect also. These include

- Soya Isoflavones
- Black Cohosh
- Elemental calcium
- Vit D
- Vit E

*Q. What is Osteoporosis? How does osteoporosis present?*

Osteoporosis basically means weak bones. Often symptomless or silent, it may present with any or all of the following

- Back pain
- Loss of height due to vertebral compression
- Spinal deformity- kyphosis
- Multiple fractures spontaneously after some everyday activity

*Q. How is osteoporosis diagnosed?*

Osteoporosis was once diagnosed only after fractures had occurred because there was no test that could determine when bone had weakened. Since then, researchers have found that the most effective way to diagnose osteoporosis is through the use of bone mineral density (BMD) measurements that can identify mineral loss in intact bone.

*Q. How much calcium and vitamin D do I need each day?*

Calcium and vitamin D are important nutrients for bone health. According to a panel convened by the National Institutes of Health, women who are still menstruating, or who are postmenopausal but taking menopausal hormone therapy, should consume 1,000 mg of calcium each day. Postmenopausal women not on hormone therapy should consume 1,500 mg/day.

*Q. Are there any other dietary ways to maintain bone?*

To help keep estrogen levels from dropping sharply after menopause, and thus help prevent osteoporosis, some practitioners advise postmenopausal women to consume more foods containing plant estrogens, especially tofu, soybean milk, and other soy products.



*Q. Is there a cure for osteoporosis?*

Although there is no cure for osteoporosis, it can be treated. The goal of treatment is to prevent fractures. Along with making lifestyle changes, there are several medication options.

*Q. What medications are available for treatment of osteoporosis?*

There are many options for treatment, however bisphosphonates have been recommended as first line of treatment for osteoporosis. However if there are other symptoms of menopause like hot flashes, you may benefit from HRT which takes care of both the problems.

*Q. What are other effective treatments available for osteoporosis ?*

Yes, there are other methods too, though not used as first choice. These include

Salmon calcitonin injections

Parathyroid hormone injections or spray

Raloxifene and other SERMS.

*Q. Is there any medication available that can be taken less frequently?*

Ibandronic acid 150 mg tablet is a bisphosphonate can be taken once a month only, by mouth, and is as effective as other bisphosphonates with the advantage of less dosing.

*Q. Who should not take Bisphosphonates?*

Patients having esophageal disease/ ulceration, gastritis, duodenal ulceration or inability to stay upright for some time may not be suitable for these drugs.

*Q. How I should take Bisphosphonates?*

The tablet should be taken on an empty stomach with a full glass of water and you should remain in upright position for more than 30 mins.

*Q. I have pain in both my knees. Is it Arthritis?*

There are many causes of knee pain with advancing age. Arthritis means an inflammation of joints. (Artho-joint; -itis - inflammation). There are 100 different types of Arthritis. The common causes are:

Osteoarthritis (OA): The commonest; the joint cartilage gradually wears away and adjacent bony changes occur. Typically seen after 50 years of age. It can occur in younger people secondary to old injury or inherited forms of disease.

Rheumatoid Arthritis (RA): Auto-immune disease; viz. immune system of patient attacking his own body, mainly the joint lining. Progressive destruction of cartilage and adjacent bones, tendons, muscles and ligaments. Generally affects younger age group.

Other causes: Gout (high uric acid), Psoriatic arthritis, infective arthritis.

*Q. What is the role of exercise in treatment of OA?*

Studies show that exercise is one of the best treatments for osteoarthritis. Exercises improve mood and outlook, decrease pain, increase flexibility, strengthen the heart and improve blood flow; thereby maintaining weight, and promoting general physical fitness. Exercise is also inexpensive and, if done correctly, has few negative side effects.

*Q. Does weight control help Arthritis?*

Osteoarthritis patients who are overweight or obese should try to lose weight. This reduces stress on weight-bearing joints, limits further injury, and increases mobility. A dietician can help you develop healthy eating habits. A healthy diet and regular exercise help reduce weight.

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