<u>A-Z OF OSTEOPOROSIS</u>

Osteoporosis literally means porous bones. It is a condition in which bone tissue is reduced and the micro-architecture of bone is disrupted. This leads to an increased risk of fracture which usually involves the spine, hip or wrist. The World Health Organisation (WHO) defines osteoporosis as a systemic skeletal disease, characterised by low bone mass and micro-architectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture.

It is a myth that osteoporosis is a normal part of aging and that only women are susceptible. We now know that this disease can also affect young people as well as men.

Osteoporosis is called the *silent disease* because it progresses undetected for many years and the first sign of this disease is usually a fracture. Spinal fractures may be painless, but often result in severe back pain for several weeks. Compression fractures of the spine occur because the weakened bone collapses under the body's weight. This causes a loss of height and increased curvature of the spine (Dowager's hump).

The majority of hip fractures is also the result of osteoporosis and can be a devastating consequence – resulting in institutionalisation, reduced functional capacity and even death. Hip fracture rates in South African Caucasians are similar to those in Europe and the USA.

Some Fast Facts About Osteoporosis

- More than one-third of women over the age of 50 and nearly half of those over age 70 are affected by this disease.
- Osteoporosis in men is on the increase, and one in 5 men will develop this disease.
- In most cases the patient is 50-70 years old before osteoporosis is diagnosed- it can however, affect women and some men in their mid thirties or even earlier.
- Without appropriate preventative therapy, one out of every three White and Asian post-menopausal women will have a spine fracture.
- A woman's risk of sustaining a hip fracture is equal to the combined risk of developing breast, uterine and ovarian cancer.
- Up to 20% of hip fracture victims die within one year; 15-25% will require institutionalisation and less than half will regain full functional capability,
- In developed countries, spinal osteoporosis is 6 times, and hip fractures 2-3 times more common in women than men – in developing countries, including South Africa, the incidence of hip fractures in men approximates that of women. Although less common in blacks, osteoporosis occurs in all population groups and recent evidence suggests that its prevalence is increasing.
- Although treatable, the prevention of osteoporosis is much more effective. This

requires an understanding of predictive factors so that the likelihood of osteoporosis may be judged, an awareness of methods to measure bone mass, knowledge of lifestyle adaptations, and drugs available to prevent further bone loss.

• Recent advances in treatment options have resulted in a 50-70% reduction in the rate of osteoporotic fractures

Who Is At Risk?

Osteoporosis can be divided into two types: primary and secondary osteoporosis. **Primary osteoporosis** is the more common. **Secondary osteoporosis** is usually the result of an identifiable agent or disease process that causes the bone loss.

Although the exact cause of primary osteoporosis is not always clear, a number of risk factors are known to increase the chances of developing this disease.

Remember - an individual may have these risk factors and not develop osteoporosis. Conversely, many people may have no apparent risk factors and develop osteoporotic fractures.

RISK FACTORS FOR OSTEOPOROTIC FRACTURES

(A) DECREASED BONE STRENGTH

(i) Genetic Factors

Elderly females Family history of osteoporosis White, Asian and Mixed - race origin Excessive leanness

(ii) Lifestyle Factors

Alcohol abuse Heavy smoking Malnutrtion Sedentary lifestyle Chronic immobilisation Excessive exercise plus low energy intake

(iii) Diseases/Drugs

Hormonal disorders (Cushing's; hypogonadism; hyperthyroidism; type I diabetes). Malignant diseases (e.g myeloma; solid tumours)

Gut disorders (e.g. Gastrectomy; inflammatory bowel disease; malabsorption syndromes)

Collagen disorders (e.g. Rheumatoid arthritis; osteogenesis imperfecta; Marfan syndrome)

Eating disorders (anorexia nervosa; bulimia)

Drugs (e.g. cortisone; anti-convulsants; anti-coagulants; excessive thyroid hormone)

(iv) Ageing Factors

Premature menopause Osteoblast(bone building cell) incompetence Negative calcium balance resulting in overproduction of parathyroid hormone

(B) INCREASED PROPENSITY TO FALL

Mental impairment* Institutionalisation Gait and balance disorders* Weakness and immobility Visual impairment Environmental hazards/accidents History of falls

* Increased by alcohol and drugs like sedatives, anti-depressants, antihypertensive drugs and anti-diabetes agents.

Gender, Age and Race

The peak bone mass of women, which is reached at 25-30 years, is usually about 10-25% less than that of men. After peak bone mass is reached, bone mass gradually declines in both women and men. Because of the rapid bone loss during the menopause, osteoporosis occurs more frequently in women than in men, who have no well defined "andropause"- men lose sex hormones (testosterone) at a much slower rate.

Although osteoporosis is not a normal part of aging, the likelihood of developing this disease and associated fractures becomes greater the longer you live.

South African White, Asian and Coloured populations are at higher risk to develop osteoporosis than Blacks. Current research is under way to determine why.

Heredity

Genetic factors play an important role in achieving adult peak bone mass. This is apparent in females where those with mothers suffering from spinal osteoporosis, tend to have lower bone densities.

Peak bone mass can however be influenced by calcium intake, exercise, hormonal factors and general health.

Body Build

Short, small framed individuals with low body weight have less bone to lose than larger, big boned women.

Fat tissue is an important source of estrogen production - petite women often have lower blood levels of this bone protective hormone.

Reproductive History

The female sex hormone, estrogen, protects against bone loss. A premature menopause (before age 45), whether spontaneous, or surgically induced, markedly increases the risk of osteoporosis.

Not breast feeding also appears to incur additional risk, whereas pregnancy with its accompanying high levels of estrogen actually protects against bone loss. A rare form of pregnancy-induced osteoporosis is however, well documented.

A decrease in testosterone levels of men can also result in bone loss and osteoporotic fractures. Up to 30% of men with osteoporosis have low testosterone levels.

Diet

A variety of nutritional factors influence bone health and a balanced diet containing adequate calories, minerals, vitamins and other nutrients is required to build and maintain strong bones. Sufficient calories, protein and Vitamin C are required for normal collagen synthesis.

Excessive phosphorous, protein and salt intake may enhance the excretion of calcium in the urine.

Caffeine has still to be proven harmful to bone.

Calcium is probably the most important nutrient needed for a healthy skeleton- especially in children, pregnant or lactating women and the elderly.

Calcium is important for bone, muscle, heart, nerve and blood cells to function normally. We lose calcium in urine and stools every day. It is therefore important to balance this loss with an adequate intake of calcium. If there is more calcium loss than intake, calcium gets released from bones and a longstanding depletion can lead to a decrease in bone mass.

Vitamin D deficiency is becoming a global problem for a variety of reasons (e.g. institutionalization, use of sunblock, pollution, etc). Vitamins D aids in calcium absorption from the gut and renews and mineralizes bone tissue.

Lack of exercise

Mechanical muscle-pull on bone is the only physiological way to stimulate bone formation. Immobilisation causes a dramatic decrease in bone tissue and 20-40% of bone mass can be lost within a 2 year period. Weight bearing exercises like walking, jogging, dancing etc. are important to prevent bone loss.

Over-training in both men and women can also lead to bone loss.

Alcohol

Studies have shown that the intake of more than 2 alcoholic beverages per day can lead to osteoporosis.

Chronic alcoholism is associated with significant bone-loss in nearly 50% of cases, and alcohol has a direct toxic effect on bone.

Smoking

Women who smoke tend to have lower blood levels of oestrogen, a lower body mass and tend to go through an earlier menopause than non-smokers. Bone mass in smokers is generally 15-25% lower than non-smokers.

Medications

The long-term (more than 6 months) use of **glucocorticoids** (e.g. cortisone used for treating asthma, eczema, arthritis etc) is an important cause of osteoporosis.

Other drugs known to negatively influence bone formation include **anti-epileptic agents**, certain **diuretics**, **anti-coagulants**, **immuno-suppressive drugs** and **aluminium-containing antacids**. Patients on **thyroid hormone replacement** therapy should have there hormone levels checked regularly since excess thyroid hormone can also result in bone loss.

HOW DO I KNOW I AM AT RISK?

The treatment of advanced osteoporosis is difficult and the real key to the management of this disease is prevention. It is therefore extremely important to identify, sooner rather than later, those individuals who are at risk. Osteoporosis is a silent disease with no symptoms until a fracture occurs- to wait for symptoms is therefore too late. What can be done to predict future fractures?

1. Clinical Risk Factor Assessment

Those risk factors which may predispose to the development have already been discussed and we mention the more important ones again: Advanced age Premature menopause (before 45 years) Other causes of low sex hormone levels in men and women Long term cortisone use Previous fracture after minimal trauma Alcohol or tobacco abuse Certain hormonal, intestinal or malignant diseases Excessive leanness A strong family history of osteoporosis Malnutrition, poor calcium intake and eating disorder (e.g. anorexia, bulimia)

Although the predictive value of a clinical risk factor is not accurate (i.e. individuals without risk factors may develop osteoporosis), it provides clear indications for further investigations (e.g. bone mass measurement).

2. Bone Mass Measurement

A low bone mass is strongly associated with the development of fractures and **bone mass measurement is currently the best predictor of fractures.** Bone mass measurements should always form part of a comprehensive programme of medical management, preferably done by a knowledgeable physician.

Routine screening of bone mass without any indication is cost- ineffective and not recommended.

Indications for Bone Mass Measurement

- (i) Presence of disorders known to be bad for your bones
 - Early menopause; other causes of low sex hormones

- Hormonal, gut malignant, nutritional/eating disorders
- Bone toxic drugs
- (ii) X-ray evidence of low bone mass or fracture
- (iii) History of non-traumatic fractures
- (iv) To decide whether to start/continue with hormone replacement therapy or not
 - Presence of strong historic factors e.g.
 - Family history of osteoporosis
 - Excessive leanness
 - Alcohol abuse
 - Heavy smoking

Techniques available to measure bone mass and fractures include:

Dual-Energy X-ray Absorptiometry (DEXA)

X-ray energy is passed through the spine, hip other part of the skeleton. It is precise, accurate and painless.

Computerised Tomography

The so-called CT accurately measures spinal bones mass. To date it cannot measure hip bone mass. Compared to DEXA, the radiation dose is higher and the measurement less reproducible.

Other Methods

(v)

X-rays- Although essential to detect fractures and deformities, it is not accurate enough to detect bone loss. Up to 40% of bone loss needs to occur before it is detected on X-rays. The converse also happens where falsely positive findings for osteoporosis occur in about 25% of cases.

Single Photon Absorptiometry (SPA) - Measures bone in the wrist and forearm; this is useful but does not always provide accurate information about bone density in other sites.

Ultrasound- measurements of the heel bone or shin have much potential, but at present the technique is not recommended to confirm a diagnosis of osteoporosis or to follow up response to therapy.

3. Biochemical assessment

Biochemical tests done on blood and urine samples to assess bone turnover (the chewing away as well as the forming of new bone), are available to identify those at risk of rapid bone loss or fracture. They are also used to assess the response to therapy.

HOW CAN I PREVENT OSTEOPOROSIS

Preventive measures aim to ensure maximum accumulation of bone tissue during skeletal growth and maturation as well as reducing bone loss after the skeleton matures.

Approaches therefore differ during each life stage. Adolescence and young adulthood are the times to build skeletal reserve; midlife provides the opportunity to preserve bone mass and assure bone health in future years. In later life, those who may already have developed osteoporosis can take measures to prevent further bone loss and fractures.

Certain risk factors which predispose to the developing of osteoporosis cannot be alteredyou cannot change your gender, race or age. You can still however do much to prevent further bone loss.

Lifestyle Changes

There are 4 main areas in which you can help maintain healthy bones: Balanced diet rich in calcium/ calcium supplements/ vitamin D Regular weight-bearing exercise Stop smoking Decrease alcohol intake and avoid bone toxic drugs

Diet

A balanced diet containing adequate calories, minerals and vitamins is required to maintain bone health. Sufficient **calories**, **protein**, **and vitamin C** will ensure normal collagen synthesis.

An adequate **Calcium** intake is probably the most important bone building mineral.

It is a well known fact that the diet of most individuals in western countries like South-Africa, contain insufficient calcium to maintain a positive calcium balance.

Reasons for limited consumption include a distaste for dairy products, fear of calories and fats (although skim milk actually contains slightly more calcium than full cream milk), true milk allergy (rare in adults) and lactose intolerance which occurs frequently in the elderly, Blacks and Asians. Fermented lactose products like cheese and yoghurt are however tolerated by most.

Group	Daily intake (mg)
Infants	
Birth – 1 year	500
Children	
1 - 5 years	500
6 -10 years	800
Adolescents / young adults	1200
Adult women and men	
25 - 65 years	1000
Pregnant and lactating	1200
Over 65 years	1200

Optimal Calcium Requirements

Note:

Whereas calcium is an essential mineral required to build bone mass and to slow agerelated bone loss, calcium alone will not protect against bone loss resulting from estrogen deficiency in the post-menopausal female; it will also not provide protection against the bone loss cause by physical inactivity, smoking, alcohol abuse or bone toxic drugs. Sufficient calcium is just one of the many steps to ensure a healthy skeleton.

Calcium Supplementation

Calcium supplements should be considered when dietary intakes are insufficient. Calcium is not found free in nature and is usually bound to a salt (e.g. calcium carbonate, calcium citrate, calcium lactate etc). Since these salts all yield different amounts of elemental calcium (actual calcium that gets absorbed), it is important to know what the elemental calcium content of your supplement is, to know how much of it you should take per day.

Vitamin D enhances calcium absorption and is consumed in the diet and produced in the skin under the influence of sunlight. The recommended daily dose of vitamin D is approximately 800 international units (IU) for individuals under 70 years and 1200 IU for those over 70. Pharmacologic doses of vitamin D or vitamin D metabolites should be taken under the supervision of a doctor. Excess vitamin D may cause kidney stones

Calcium supplements are best absorbed if taken in **small amounts** throughout the day and **with meals** (calcium carbonate needs the presence of stomach acid to split from its salt, in order to get absorbed).

Avoid taking more than 500mg at one time.

Avoid taking calcium together with foods known to impair its absorption (e.g. fiber, oxalates, phytates, bulk-forming laxatives.)

Calcium supplementation is safe and generally free of side-effects- constipation can occur – increase your fluid and fiber intake, as well as exercise regularly.

There is no evidence, even in individuals with a personal or family history of kidney stones, that calcium supplementation causes kidney stones. If you take more than 2000mg per day and also in conjunction with Vitamin D, your urine calcium will increase and kidney stones may develop. Consult your doctor if this is the case and have your urine calcium levels monitored.

Exercise

Regular exercise is important at all ages as it is the only physiological way to stimulate bone formation. Individuals who exercise regularly tend to have higher peak bone mass and it also seems to slow down age-related bone loss. The exact mechanism of how exercise influences bone turnover is not known:

The muscle pull on bone generates pizo-electrical charges on bone surfaces which stimulate osteoblast activity and bone formation.

Exercise also causes the release of hormones that promotes bone formation.

Exercise stimulates blood flow within the bone.

Exercise improves balance, co-ordination and confidence- these help to prevent falls. It also strengthens muscles and flexibility, and protects against fractures even in the event of a fall.

Weight bearing exercise like brisk walking, stair climbing, jogging or dancing is better than non-weight bearing exercise like swimming or cycling, although it is excellent to start with these if you have not exercised in a while.

A brisk 45 minute walk at least 3x a week is recommended. Wear comfortable shoes with good arch and heel support.

Exercises to improve the posture and strengthen the pelvic floor, back and stomach muscles, are also very important.

Stop smoking, limit alcohol intake and avoid bone toxic drugs

The detrimental effects of tobacco and alcohol abuse on bone tissue have already been discussed. If you are serious about your health and want to prevent osteoporosis – don't abuse these bone toxic substances.

Pharmacologic Agents

Calcium and Vitamin D

Already discussed

Hormone Replacement Therapy (HRT)

HRT is used to replace those hormones which decline during the menopause. Essentially the ovaries produce two hormones namely progesterone and estrogen, although a small amount of male hormones (testosterone) are also produced. In women who have had a hysterectomy, only estrogen replacement is used. In women who still have a uterus, progesterone needs to be added to counteract the stimulating effect of estrogen on the endometrium (inner lining of the uterus) which can lead to uterine cancer.

Benefits of HRT

HRT was originally developed to relieve the symptoms of the menopause (hot flushes, night sweats, mood swings etc). It is now known that HRT also prevents the serious long-term complications of estrogen deficiency (e.g. osteoporosis).

Osteoporotic fractures of the spine, hip and wrist appears to be decreased by 50-70%.

Estrogen has a beneficial effect on blood vessels and blood cholesterol.

HRT appears to improve cognitive function and may delay the onset of Alzheimer's disease although further research is required. It significantly decreases the incidence of colon cancer.

Potential Risks of HRT (Long term use)

Cancer

Uterine Cancer

Endometrial cancer is increased in women who take only oestrogen therapy and still have their uterus intact. Progesterone should therefore be taken in conjunction with oestrogen. Combined HRT does not increase the risk of uterine cancer.

Breast Cancer

Long-term oestrogen therapy (more than 5 years) increases the risk of breast cancer. The risk seems to be insignificant in the short-term (less than5 years). Before initiating HRT, a baseline breast examination and mammogram should therefore be done.

Other cancers

The risk of other cancers is not increased.

Vascular problems

HRT is known to increase the incidence of deep vein thrombosis (DVT). HRT should be temporarily discontinued during periods of relative immobilisation (e.g. bed rest, long flights).

Recent evidence has suggested that there may be an increased risk of cardiovascular disease during the first year of HRT. Known coronary artery disease and a recent myocardial infarction (heart attack) should be regarded as a contra-indication for HRT.

(Short term side-effects)

Vaginal bleeding

This usually occurs when HRT is given cyclically (10-14 days per month) and a monthly bleed follows. HRT can also be given continuously. Bleeding may occur for the first 6 months and should stop. If it continues, this needs to be investigated.

Breast discomfort

Breast discomfort and enlargement can be quite bothersome. It usually decreases with time and can be overcome by changing the hormone preparation or reducing its dose.

Fluid retention

This is more frequent in women who have been without oestrogen for many years and are started on too high a dose of HRT. These symptoms usually disappear after a while. Reduce salt intake and exercise. A different hormone preparation and the addition of a diuretic can also relieve symptoms.

Contra-indications

Absolute contra-indications

Cancer of the breast and uterus Unexplained uterine bleeding

Pregnancy Active liver disease Recent or active vascular thrombosis

Relative/Potential contra-indications

History of previous thrombo-embolic disease Poorly controlled hypertension Recent myocardial infarction Strong family history of breast cancer Porphyria Uterine fibroids, endometriosis, migraine, epilepsy

Who should take HRT?

HRT remains the only true effective way of treating the symptoms of menopause and is still one of the most cost-effective ways to prevent post-menopausal osteoporosis- it reduces fractures of the spine and hip by 50%.

It does however have side-effects and is not suitable for every woman. Decisions whether to start with HRT should be based on a thorough knowledge of the subject and open and honest discussion between the patient and her doctor. Every patient should be treated as an individual with specific needs.

Safe and effective alternatives to HRT exist to prevent osteoporosis.

TREATING OSTEOPOROSIS

Never accept the incorrect and uninformed advice that "osteoporosis is a normal part of aging" or that "nothing can be done". There are many treatment options available to reduce bone loss. Many of these potent drugs are capable of reducing the rate of osteoporotic fractures by 50% or more.

Specific Medical Treatment * (List of available drugs below)

The aim of specific medication used in the treatment of established osteoporosis is to stop further bone loss, to replace or repair bone and to prevent further fractures. These drugs can be divided into two broad groups- those that inhibit bone resorption (chewing away of bone) and those that stimulate bone formation (building new bone).

Anti-resorptives serve mainly to slow bone breakdown and include calcium, vitamin D, oestrogen, SERM's, bisphosphonates and calcitonin. They act primarily to maintain bone mass.

Bone- formation stimulating drugs aim to increase bone mass and include fluoride, anabolic steroids, strontium salts, statins and para-thyroid hormone.

Anti-Resorptive Drugs

Calcium

All patients with osteoporosis should ensure a calcium intake of at least 1000-1500mg per

day- especially the elderly where a 25% reduction in the incidence of hip fractures has been reported following calcium supplementation.

Vitamin D and Vitamin D-metabolites

Low dose vitamin D (400-800IU/day) will ensure adequate calcium absorption in healthy, young individuals. In the elderly, housebound patient larger doses of vitamin D (50,000IU every two weeks) may have to be considered. Vitamin D has also been shown to improve muscle strength and co-ordination. When high doses of vitamin D is taken, blood and urine levels of calcium may rise and cause kidney stones. Careful monitoring by a physician is imperative.

Vitamin D metabolites (calcitriol, alfa- calcidiol) have been shown to decrease the rate of spine fractures

Conventional Hormone Replacement Therapy

HRT is most effective in maintaining bone mass within the first 5-10 after the menopause and can prevent fractures by almost 50%. It is however not recommended as first line treatment (as opposed to the prevention) of osteoporosis.

Oestrogen derivatives, selective oestrogen receptor modulators (SERM's), phyto-oestrogens and testosterone

SERM's like raloxifene have oestrogen-like effects on bone and lipids and anti-oestrogen effects on the breast and uterus. It is not associated with menstrual bleeds and breast cancer. Hot flushes are the most common side effect and it carries the same risk for venous thrombosis as HRT.

The synthetic steroid derivative **tibolone**, has mild oestrogenic, progestogenic an androgenic properties.

The use of **progesterone** on its own is not recommended for either the prevention or treatment of osteoporosis.

Plant or **phyto-oestrogens** may improve menopausal symptoms, but no data on the prevention of fractures are known.

Experimental data exist that **testosterone** has beneficial anabolic effects on bone tissue. Under certain circumstances, testosterone supplementation may be indicated in women.

Approximately one-third of men with osteoporosis has low levels of testosterone and requires replacement.

Bisphosphonates

The bisphosphonates (e.g. alendronate, risedronate) are potent, extremely effective, nonhormonal anti-resorptive drugs which act directly on bone. They can reduce both spine and hip fracture rates by more than 50%.

Bisphosphonates are usually well tolerated, although upper gastro-intestinal side-effects occur in about 5-10% of patients. The drug should be taken with a full glass of water at least 30 minutes before having food or beverages and the patient should remain upright for this period.

Calcitonin

Calcitonin is a naturally occurring hormone produced by the thyroid gland. It slows bone breakdown (resorption) and studies has shown that it decreases the rate of vertebral fractures. It is administered by injection or as a nasal spray and has an added benefit of providing pain relief - it is therefore often used in the treatment of acute fractures.

Formation Stimulating Drugs

Fluoride

Fluoride is administered as a slow- release enteric coated formulation. Side-effects include gastric irritation and joint pains. Response to therapy varies and treatment with this drug should best be done by an expert. Adequate calcium and vitamin D should always be taken with this drug.

Anabolic Steroids

Anabolic steroids are synthetic derivatives of the male hormone testosterone. They stimulate bone formation, decrease bone resorption and improve muscle strength. These agents are usually reserved for the short term (< 12 months) treatment of patients with advanced osteoporosis, especially the frail and elderly where muscle strength is impaired. Side effects (masculinisation in females, water retention and abnormal liver functions) appear to depend on the cumulative dose as well as individual sensitivity.

Parathyroid Hormone

This drug has been available in South Africa for the past year and also stimulates bone formation and inhibits bone resorption. It increases bone mass and bone strength and significantly reduces the risk of hip and spine fractures. Parathyroid hormone (PTH 1-34) is given as a daily sub-cutaneous injection for 18 months. It is unfortunately very expensive and used to treat severe osteoporosis.

Statins

Statins (cholesterol lowering drugs) may stimulate bone-formation. Further studies are needed before these drugs can be used to treat osteoporosis.

Strontium

Strontium ranelate stimulates bone formation and inhibits bone resorption – thus increasing bone mass and bone strength.

Lifestyle Adaptations

The lifestyle adaptations discussed in the prevention of osteoporosis is just as important in the treatment of osteoporosis i.e. exercise, a calcium rich balanced diet, stop smoking and limit alcohol intake.

If you have osteoporosis, you may be wondering whether you should exercise at all. Certain exercises can safely strengthen your back and stomach muscles, as well as help to maintain normal flexibility and balance. Check with your doctor or physiotherapist before embarking on your own exercise programme.

* Trade names of available drugs

SERM's/Raloxifene	Evista
Tibolone	Livifem
Bisphosphonates	Actonel, Fosamax, Aclasta once yearly infusion
Calcitonin	Miacalcic
Fluoride	Ossiplex Retard
Parathroid Hormone	Forteo
Strontium Ranelate	Protos

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