Osteoporosis – an increasingly important issue for both young and aging citizens of Malaysia

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"The great secret that all old people share is that you really haven't changed in seventy or eighty years. Your body changes, but you don't change at all. And that, of course, causes great confusion."

Doris Lessing, born 22 October 1919.

- The Sunday Times, London (10 May 1992). -

In both sexes, peak bone mineral density (BMD) occurs in early adulthood.[1] Thereafter, there is a gradual decrease in BMD which is hardly noticeable until the middle years, and which in a significant proportion of the population leads to an incipient osteopenia that may eventually progress to frank osteoporosis. Such gradual change is but one of a plethora of slow functional declines in tissue activity that start in early middle age and inevitably contribute progressively to morbidity in the aged.

Osteoporosis is generally a silent disease, undiagnosed until what would otherwise be a minor trauma from a fall, results in a fracture. While an osteoporosis-associated fracture can occur almost anywhere in the skeleton, the most significant sites are the wrist, the vertebrae, and the head or neck of a femur: these are the sites that are usually subjected to the greatest stress from an accidental fall.

A hip fracture degrades mobility and causes a great deal of pain, so a hip fracture is the most serious consequence of osteoporosis, because it carries a 24% risk of mortality in those over 50 years of age,[2] which rises to 51% in nonagenerians.[3] Osteopenia and osteoporosis generally affect women (75%) to a greater extent than men (25%). This gender imbalance is a consequence of three primary factors: firstly, women achieve a lower peak BMD than men; secondly, this declines rapidly from early menopause[4]; and thirdly, in almost every population, women have a longer life expectancy than men, and as a consequence there is a steadily increasing proportion of women with increase in age. Karim (1997)[5] has indicated that the percentage of females in the population of Malaysia of 70 years and over was 54.2% in 1990 and has estimated that it will increase to 56.7% by 2020. According to the New Straits Times for February 19, 2013, "Life expectancy for Malaysian women is expected to reach just above 79 years while Malaysian men could expect to live until 74.2 years, by the year 2020".

According to Morrison *et al.*,[6] 1.4% of the community-dwelling elderly in the US experience an osteoporosis-related fracture annually. While these figures are somewhat higher than those for East Asian populations, they are never the less indicative and likely to be met or superseded in Malaysia in future years as the population ages further. The age-adjusted rates for hip fracture in the Malaysian population aged over 50 (per 100,000) are stated to be 88 for men, and 218 for women.[7] These figures translate to a 5.2% lifetime risk for a woman living to an average female life expectancy of 74 years. Hence a fracture induced by osteoporosis is likely to be a primary cause of mortality for at least 2.6% of the female population of Malaysia. All these considerations suggest that while few adequately detailed clinical studies have been undertaken in Malaysia to make accurate predictions, the next decade will see a strong increase in osteoporosis-related trauma and resulting morbidity.

In June 2012, the Clinical Guidance on Management of Osteoporosis Committee Working Group of the Malaysian Osteoporosis Society, under the chairmanship of Drs Chan Siew Pheng and Yeap Swan Sim, developed some very comprehensive and timely guidelines for the clinical assessment and management of osteoporosis. However, these guidelines basically attack the problem from an "ambulance at the bottom of the cliff" perspective. A seriously traumatic fracture in an elderly person inevitably results in a severe decline in quality of life: it is not practicable to effectively restore this to its status before the accident. So if rates of osteoporotic fracture and resulting morbidity are to be minimised (or hopefully to decrease), the main thrust of concern has to move from treatment to prevention. One major obstacle to achieving this is Nature herself. While the relative contributions of genetic versus

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socio-environmental components of osteoporosis are always going to be subject to debate, never the less, genetic factors are important in determining individual susceptibility to osteoporosis. Genetic susceptibility cannot be changed, but it can be assessed through analysis of a proband's genetic polymorphisms, and countered. A great number of candidate genes which convey increased susceptibility (or resistance) to osteoporosis have been identified: as long ago as 2002, this list already totalled 25 genes.[8] Since then, the number has greatly increased, through the application of new genetic approaches; for example, an analysis of genes in chromosome 1p36 that are linked to bone mineral density.[9] Knowledge of the contributions of specific candidate genes to the overall susceptibility of a patient to osteoporosis point the way to the development of appropriate genetic markers for assessment of risk of osteoporosis, the identification of targeted drugs for the specific suppression of expression of unfavourable markers, and the development of both general, and specific patient-directed, treatments for osteoporotic bone disease. Such developments are now on our doorstep.

What are the medical community in Malaysia, X-ray departments and medical diagnostic labs doing to turn these expectations into reality? The priorities are clear - in summary:

1. To maximise BMD for the population at all ages as far as possible, by disseminating and encouraging necessary modifications in dietary practice designed to increase calcium dietary uptake, and by actively supporting changes to encourage appropriate weight-bearing activities and exercise.
2. To provide adequate facilities for screening bone mineral density in all populations at risk of osteopenia, and at an age when there is still a good likelihood of effecting an increase in BMD through appropriate interventions, long before a fracture has starkly revealed the problem.
3. To institute adequate genetic screening to identify subjects who are at a particularly high risk of development of osteoporosis, so that these subjects can receive specific advice or medical interventions.
4. To minimise risk of fall in the elderly by assessment of specific risk through home visits from occupational therapists, followed by the implementation of any resulting improvements (such as guard railings, ramps, etc), and through provision of specific aids to help in safe mobility.

In terms of the time-course of prevention, osteoporosis takes decades to develop. As pointed out by the Clinical Guidance Working Group, one of the important factors in determining peak bone density is dietary calcium intake. Malaysians typically consume only about half of the recommended levels for calcium in the diet, with intakes of around 470 mg/day in the case of post-menopausal Chinese women from West Malaysia.[10] It is during the pubertal growth spurt that the bone density of a pre-adult appears to be largely determined. It is clear that a substantially increased intake of calcium from childhood onwards would do much to improve peak bone density, and thereby minimise the potential for osteoporosis in later years. The main source of dietary calcium throughout the globe is milk products. What is being done to encourage Malaysians of all ages to consume milk and dairy products such as cheese and yoghurt on a day by day basis? While there has been a good start in the provision of milk to the majority of 6-12 year-old schoolchildren through the Malaysian Government's School Milk Programme, there is no such provision in secondary schools or in private schools, at a stage in skeletal development when a high calcium intake is especially important.

A second area where a programme of active intervention would help is specialised support aimed at the identification and minimisation of the risks of fracture for elderly people. Eyesight, balance, muscle strength and neuronal function are often deteriorating in the elderly. All of these adversely increase the risk of a traumatic fall. Simple modifications and repairs to pathways, provision of railings and availability of appropriate

walking aids will help to minimise such accidents. Such lifestyle interventions are traditionally the domain of occupational therapists, visiting the homes of elderly people and advising suitable improvements to safety, then implementing the necessary changes through local or central government-supported modifications. Is this sort of programme being instituted widely in Malaysia or even envisaged for the future?

The "gold standard" means of immediately and directly assessing osteoporosis risk is bone mineral density measurement through dual X-ray (DEXA) scanning of the hip and lumbar spine. While DEXA machines are generally available in main city hospitals in Malaysia, a substantial proportion of the population lives well outside the coverage areas. Performing these scans to a high level of reliability requires well-trained technicians. Purchasing enough of the appropriate X-ray equipment to reach the whole population would be expensive. Can it be done? If so, when will it be done?

Finally, there have been major advances in phamacotherapy for osteoporosis in recent years, and these have been expertly highlighted in the guidelines for the clinical assessment and management of osteoporosis, discussed above. One of the most promising approaches is administration of denosumab, a human monoclonal antibody directed to receptor activator of nuclear factor-κB ligand (RANKL). This antibody interferes with the recruitment of osteoclasts, thereby reducing bone resorption, and is administered as a subcutaneous injection every few months. At 36 months of treatment, denosumab was found to be associated with reductions of 68% in vertebral fracture and 40% in hip fracture.[11] The availability of this treatment in Malaysia, both for treatment of osteoporosis and for its ancillary application, to suppress bone metastases, is currently unclear.

So, in summary, there is evidence that rates of osteopenia and osteoporosis will almost inevitably increase in the short-term future. Osteoporosis takes many years of slow and insidious imbalance between osteoblastic bone deposition and osteoclastic bone resorbing activities to develop to the point where there is a real risk of morbidity associated with fracture in elderly people. What is Malaysia doing to prevent this incipient epidemic? If the answer is "not enough", then the time for change to this situation has come with the huge expansion of knowledge of the causes and the variety of means of avoidance, diagnosis and treatment of this distressing disorder which has become clear in recent years. While osteoporosis cannot be eliminated entirely, there are now many complementary strategies for decreasing its prevalence. Perhaps the time to be enthusiastically pursuing these strategies for the benefit of both young and not-so-young members of the wider Malaysian community is NOW.

Keywords: osteopenia; osteoporosis; bone mineral density; neck of femur; fracture; denosumab; fall prevention; DEXA.

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