5th South African Menopause Society Congress

2 - 5 March 2006, Sun City

RHEUMATISM AND ARTHRITIS IN THE MENOPAUSAL FEMALE

Ingram F. Anderson
Rheumatologist, Pretoria

Apoptosis of the last of the ovae in a middle-aged female signals remarkable endocrine changes with protean manifestations. In the musculo-skeletal system, these changes are dominated by the advent of osteoporosis.

Some rheumatic diseases appear to be more common in the menopausal period. Certain criteria need to be applied for inferring causality between menopause and a disease:

the association is unlikely due to chance
the association cannot be explained by bias
the menopause precedes the onset of the disease
the association is biologically explicable
the association is shown to be:

- strong
- consistent in different studies
- related in a dose-response manner
- supported by animal or in-vitro work
- supported by changes in the exposure altering the risk of disease
- supported by geographic and temporal relationships.

Certain disease however do seem to be more common and/or different in the middle-aged woman. The following points will be dealt with:

- osteoarthritis
- gout
- idiopathic hemochromatosis
- hormones and rheumatoid arthritis

Is the future then of the menopausal female so dark that we have to admonish them to "Go not gentle into the good night, but rage, rage against the dying of the light".

ADVANCES IN BREAST HEALTH MANAGEMENT

J. Apffelstaedt
University of Stellenbosch

In the third millennium, breast cancer management is becoming more biological and personal.

Computerized risk assessment models allow the rapid analysis of the individual patient's pedigree and her biologic risk factors. The breast cancer risk is given as an estimate over 10 years and life-time versus the normal population. Likewise, probabilities for the presence of a BRCA 1 or 2 abnormality are estimated. Personalized risk management strategies can then be developed. These may include increased surveillance, chemoprevention or risk reduction surgery.

Better understanding of the biology of recurrence after breast conservation, which may reflect a field defect in the area of the primary tumor rather than a predisposition of the entire breast to malignant transformation has led to the development of the concept of partial breast irradiation. Here, only the tumor bed is radiated. Broadly methods can be divided into modified external beam ("outside in") techniques and techniques, where the radiation source is placed in the tumor bed ("inside-out") techniques. All techniques reduce the fractions given versus conventional external beam; most radically in the intra-operative techniques where the entire radiation is give in one single dosage. With follow-up only medium term at present, the results are excellent. In South Africa, only Prof. Apffelstaedt at the University of Stellenbosch has been running such a program for the past 4 years.

With conventional chemotherapy reaching the limits of toxicity and hormonal agents reaching the end of their development potential with the introduction the Aromatase inhibitors, new biologic agents are the next major advance. About 30% of breast tumors express on their surface EGF receptors. Herceptin, an antibody against these receptors, has recently been shown to reduce recurrence rates by 50% versus aggressive anthracyclin – taxane chemotherapy in these very aggressive tumors. It is the first effective biologic agent in breast cancer to reach the market. In South Africa, it is available in the private sector.

Systemic therapy for breast cancer has for the last 30 years been directed by tumor size, lymph node involvement and differentiation of the primary tumor. These rather mechanistic parameters allowed only a very rough estimation of the patient's prognosis. Translational profiling of the tumor, in contrast, measures directly the genetic make-up of the tumor and has affords a much more accurate estimation of the prognosis. Utilization of transcriptional profiling versus traditional prognostication may save about one third of women who have been recommended to have chemotherapy, such therapy as their tumors are not aggressive. Transcriptional profiling therefore personalizes systemic therapy. It also holds the promise of the identification of targets for further biologic interventions. Transcriptional profiling of breast tumors has become available in South Africa in February 2006 through GeneCare. It requires fresh tumor samples to be taken.

HORMONE REPLACEMENT THERAPY AFTER BREAST CANCER

J S Bagratee

Most breast cancer survivors are menopausal at the time of diagnosis or are rendered menopausal as a result of adjuvant therapy for their breast cancer. The majority of these women experience quality of life problems including vasomotor symptoms and vaginal dryness related to estrogen deficiency. HRT use is controversial because of the risk of recurrence. The HABITS and Stockholm studies will be highlighted and we shall consider the evidence based literature regarding the alternatives for symptom relief.

FRAILTY AND THE MEDICAL MANAGEMENT OF OSTEOPOROSIS IN OLD AGE

S. Boonen
Leuven University Center for Metabolic Bone Diseases and Division of Geriatric Medicine, Katholieke Universiteit Leuven, Belgium

Osteoporosis is a major public health problem in old age. Most types of osteoporotic fractures increase in incidence with age and the number of elderly individuals affected with osteoporosis is expected to increase dramatically in

Selected abstracts (received by *SAJOG* by 13 February 2006).

the coming years. Women over 80 have the highest risk for fracture because 60-70% of these women have osteoporosis and falls are common. Overall, over 30% of all fractures and 60% of all hip fractures occur in this age group.

Given that a significant proportion of elderly individuals suffer from more severe osteoporosis manifested by very low bone density and an increasing number and severity of fractures, bone anabolic agents provide a therapeutic option for these high-risk patients. When comparing the relative treatment effects of teriparatide in a prespecified analysis in women <75 years of age versus those ≥ 75 on markers of bone turnover, bone mineral density and (vertebral) fracture risk, no significant differences were observed between the age groups. However, owing to the small number of nonvertebral fractures in the ≥ 75 years old subgroup, this analysis was not sufficiently powered to show a statistically significant reduction in the risk of nonvertebral fractures in elderly women. In a retrospective analysis in women over 80 with osteoporosis, risedronate significantly reduced the risk of new vertebral fractures over 1 and 3 years. These reductions in fracture risk in the risedronate-treated women were in addition to any benefit experienced as a result of calcium and vitamin D supplementation, providing the first evidence of a benefit of antiresorptive treatment in addition to that afforded by calcium and vitamin D in a population of women over 80 with osteoporosis. A treatment effect on nonvertebral fractures was not seen in these patients over 80. Although inadequate statistical power may again have contributed to the failure to demonstrate a significant effect, little evidence currently exists to support the efficacy of bisphosphonates to reduce the risk of nonvertebral fractures in women 80 years of age or older. More recently, the efficacy of strontium ranelate in elderly patients was assessed in a preplanned pooled analysis of those women who were over 80 years of age in the main clinical studies. In this analysis, strontium ranelate was found to reduce the risk for vertebral and nonvertebral fractures, both at one year and at three years. With these findings, strontium ranelate is the first drug to demonstrate an early and sustained reduction for both vertebral and non-vertebral fractures in very old patients with documented osteoporosis. These findings have important clinical implications because, as age advances, nonvertebral fractures contribute increasingly to the burden of osteoporosis. In the analyses with teriparatide, risedronate and strontium ranelate, the incidence of adverse events was not affected by age. Because a high proportion of elderly women with osteoporosis have multiple comorbid conditions, evidence for drug safety in this frail population is critically important.

Despite the debilitating effects of osteoporosis fractures and the availability of therapies to reduce fracture incidence, many elderly patients do not receive treatment, with treatment rates ranging from 5 % to 69% and decreasing with increasing age. One explanation for this decrease is the perception that it is too late to alter the course of the disease in its late stage. Given the known anti-fracture efficacy and safety of available drugs, lack of appropriate and needed therapy in patients with osteoporosis will continue to result in costly and debilitating fractures.

DESIGNER VAGINAS

Linda Cardozo

In recent years there has been growing interest in the subject of cosmetic vaginal surgery, which parallels the ever-increasing public awareness of cosmetic surgery generally. Despite the large number of articles in the popular press on this subject, there is very little evidence in the peer-reviewed medical literature to guide gynaecological surgeons on possible surgical procedures and their outcomes. An internet search using the Google search engine yields over 45,000 references to 'cosmetic vaginal surgery' whilst a search of PubMed or Medline reveals less than one hundred. The majority of the papers in the medical literature are related to the correction of congenital cloacal anomalies or intersex conditions rather than purely 'cosmetic' reconstructive surgery in women with normal genital tracts. A wide variety of surgical procedures can be included in the term 'cosmetic vaginal surgery' ranging from purely aesthetic operations like labiaplasty, hymenoplasty and 'vaginal rejuvenation' to the more conventional gynaecological reconstructive procedures like vaginal pelvic floor repair, which aim to restore function as well as enhance appearance.

Many of the claims made by surgeons who advocate this type of surgery are unsubstantiated by clinical trial evidence. As well as purporting to restore normal anatomical relationships following the effects of childbirth and ageing, some surgeons offer the promise of enhanced sexual gratification as a result of these procedures. Other than testimonials from 'satisfied clients'; there is currently no objective evidence to back this up. Indeed, most of the published literature on reconstructive pelvic surgery suggests that repeated vaginal surgery risks causing scarring, loss of sensation and decreased sexual function[1,2]. If sexual dysfunction is the primary reason for seeking surgical intervention, then it is often more appropriate to consider other avenues of treatment first, including psychosexual counselling and pelvic floor physiotherapy.

In considering how best to restore normal pelvic anatomy and function, it is important to consider all three pelvic organ systems – urinary, genital and gastrointestinal. Appropriate pre-operative assessment of function and the degree to which normal pelvic floor support has been lost is important in planning the most suitable type of surgical procedure. As well as the traditional methods of 'doctor-centred' assessment, there is currently an increased awareness of the need to formally evaluate the mental and physical impact of any condition on the patient's Quality of Life (QoL). Condition-specific sexual dysfunction QoL questionnaires have been designed and validated for this purpose[3].

In order to provide women with realistic expectations, a thorough pre-operative discussion about the aims and likely outcomes of any planned vaginal surgery is invaluable. This may sometimes need to include a careful psychological assessment of their motivations in requesting surgery over more conservative treatments.

[1]Kahn MA, Stanton SL. Posterior colporrhaphy: its effects on bowel and sexual function. Br J Obstet Gynaecol. 1997 Jan;104(1):82-6.

[2]Weber AM, Walters MD, Piedmonte MR. Sexual function and vaginal anatomy in women before and after surgery for pelvic organ prolapse and urinary incontinence. Am J Obstet Gynecol. 2000 Jun; 182(6): 1610-5.

[3]Rogers RG, Kammerer-Doak D, Villarreal A, Coates K, Qualls C. A new instrument to measure sexual function in women with urinary incontinence or pelvic organ prolapse. Am J Obstet Gynecol. 2001 Mar;184(4):552-8.

LESS INVASIVE SURGERY FOR STRESS URINARY INCONTINENCE

Linda Cardozo

Stress urinary incontinence is the commonest type of urinary incontinence. Overall approximately half of all incontinent women complain of pure stress urinary incontinence and 30-40% of mixed symptoms of stress and urge incontinence. Recent improvements in our understanding of the underlying pathophysiological mechanisms responsible for urinary incontinence in women have led to the development of innovative new medical and surgical treatment. Women of all

ages can be offered a choice of safe, effective treatment for stress urinary incontinence.

A conservative approach is still justified as first line, especially if symptoms are only mild, or easily manageable. Physiotherapy represents an effective non-invasive option for treating stress urinary incontinence. Pelvic floor exercises have been shown to be more effective than no treatment, electrical stimulation and vaginal cones and are definitely most beneficial if taught on a one to one basis by a Specialist Physiotherapist.

There is now a pharmacological treatment for stress urinary incontinence. Duloxetine has been specifically developed for this indication and has been shown to be both effective and safe. It can be given either on a short term basis for women who have not yet completed their family or are awaiting surgery or as a long term treatment regimen and is probably most effective if given in combination with pelvic floor muscle training.

There has been a recent explosion in the development of new, less invasive surgical procedures for the treatment of urodynamic stress incontinence. They claim to offer improved safety and shorter hospital stays, whilst maintaining the efficacy of traditional open incontinence surgery. It is however important that all new surgical procedures undergo comprehensive evaluation, including accurate reporting of complications, prior to being adopted for widespread use. This is best achieved by large scale randomized trials with long term follow up, comparing new procedures with tried and tested surgical techniques.

Until the end of the last century, the "Gold Standard" was the Burch colposuspension which is still performed in recurrent or complex cases and can be carried out as an open procedure or laparoscopically. However, this has been largely superseded by the mid-urethral tapes of which only the Tension Free Vaginal Tape (TVT) has been compared to the colposuspension in a randomized controlled trial. The results of this study, at two years, showed no difference in efficacy between the two techniques and no difference in the complication rates, although hospital stay and return to normal activities were significantly shorter with the TVT. Approximately a million TVT's have been inserted worldwide with follow up data up to eight years now available.

There are a significant number of similar procedures which have been introduced without such clinical trial data and most recently the Trans-Obturator Tapes (TOT) have been introduced on the basis that they may be safer and quicker to perform than the retropubic mid-urethral tapes. However, this has not been proven and there are no long term study results available.

There has also been increased interest in the use of injectable "bulking agents" and although these may not offer the same cure rate as the sub-urethral tapes, they can be used in the out patient setting under local anaesthesia and repeated if necessary.

Whilst the trend toward less invasive surgery for stress urinary incontinence is laudable, it is important that efficacy and safety are not compromised and that the treatment for this common condition is tailored to suit the individual woman after appropriate and thorough assessment of her symptoms and expectations.

VERTEBRAL FRACTURE ASSESSMENT BY DXA (VFA)

Tobie de Villiers

The aim of osteoporosis management is the prevention of fractures. The assessment of fracture risk is thus essential in the determination of a threshold for intervention with the various pharmacological agents available. The assessment of risk for fracture by DXA alone, using a T-score of lower than minus 2.5 as the threshold for intervention, will not capture all patients at risk. In order to enhance fracture risk assessment, DXA needs to be complemented by other risk factors. The presence of existing vertebral fractures, more specifically the amount and severity of the fractures, are extremely valuable predictors of fracture risk, especially when combined with DXA. The majority of vertebral fractures are asymptomatic. The conventional method of diagnosis entails a lateral X-ray of the thoracic and lumbar vertebrae. A skilled radiographer according to the semi-quantative method of Genant must read this. Unfortunately, logistical problems result in most patients not being evaluated in this way. Vertebral fracture assessment by DXA now offers a good alternative way, at the point of service. VFA adds less than 5 minutes to the standard DXA examination with minimal radiation exposure. A single image of the thoracic and lumbar vertebrae is obtained. The lecture will explain how these images are obtained and interpreted. The validation of VFA when compared to conventional radiography by various authors will be discussed. Local experience with VFA when compared to X-rays read by international expert radiographers will be presented. The limitations of VFA will be discussed. It is concluded that VFA by DXA can now be regarded as a new standard of care in the management of osteoporosis.

THE PLACE OF MENOPAUSAL HORMONE THERAPY IN THE PREVENTION AND TREATMENT OF OSTEOPOROSIS

M Davey

The Women's Health Initiative Study confirmed that E/P therapy significantly decreased the risk of both vertebral and hip fractures. In spite of this finding, the authors concluded that there was no place for the use of E/P therapy where treatment of osteoporosis was the primary indication for treatment. This conclusion was based on the finding that the Global Hazard Ratio (sum of benefits vs risks) was unfavourable for E/P use even in patients at highest risk for fracture.

A further problem with the use of Estrogen (E) or E/P therapy for the treatment of osteoporosis is the finding of many studies that the increase in density seen whilst taking this therapy is quickly lost on cessation of hormone use. In order to prevent fractures, hormone therapy would therefore have to be taken long-term, and most present guidelines advise against this because of concerns about breast cancer and vascular disease.

Certain studies have however suggested that there may be long-term bone protection with short-term use of E or E/P therapy. In addition new ways of administering menopausal hormone therapy offer promise of a different breast and vascular profile. This includes the use of low and ultra-low-dose therapy, the use of different routes of administration, the use of unopposed estrogen and the use of different progestins.

Although currently the balance of evidence supports the conclusion that menopausal hormone therapy should not be a primary treatment for osteoporosis, a reappraisal of recent in vitro and clinical data suggests that, with correct individualization, both as regards patient selection and hormone choice, there may well be a future for E or E/P therapy in decreasing the risk of fractures.

ANDROGENS AND ANTI-ANDROGENS IN MENOPAUSAL PATIENTS

Franco Guidozzi

Department of Obstetrics and Gynaecology, University of the Witwatersrand and Johannesburg Hospital

There is increasing evidence to suggest that many postmenopausal women experience symptoms that respond to

androgen therapy and that such symptoms may be secondary to androgen deficiency. Affected women complain of fatigue, low libido and diminished well-being, symptoms easily and frequently attributed to psychosocial and environmental factors. When such symptoms occur in the setting of low circulating bioavailable testosterone, testosterone replacement results in significant improvement in quality of life. Testosterone replacement for women is now available in a variety of formulations namely oral, transdermal gels, creams or implants. Research to date has demonstrated that androgen therapy leads to improvement in libido and sexual function, mood and well-being. Other potential benefits include preservation of bone mass, a possible protective role in breast cancer and beneficial effects on cognition. Adverse effects of androgen treatment are dose-dependent and include virilisation, mood disturbance and acne. These however are uncommon if appropriate doses are administered.

Several new progestogens have been synthesized in the last decade that have anti-androgenic properties of which cyproterone acetate is the most potent, followed by dienogest, drosperinone and chlormadione. These avoid many of the androgenic side effects related to testosterone-derived progestogens which will be emphasized in the presentation

THE RATIONALE FOR LOW-DOSE HORMONAL THERAPY LAUNCH OF PREMELLE L.D.

Franco Guidozzi

Department of Obstetrics and Gynaecology, University of the Witwatersrand and Johannesburg Hospital

Recent studies have shown that the dose-response curve seen with estrogens in a number of body systems, including bone, may not be as steep as initially thought, especially when progestogens are added to lower estrogen doses. As a result, there is growing interest in, and acceptance of lower-dose HRT. The anticipation is that as the dose of oral estrogen and progestogens is lowered, the benefits can be maintained and the side effects reduced. ERT or HRT with lower hormone doses may also enhance compliance with therapy, allowing a greater number of postmenopausal women to achieve the short-and long-term benefits of treatment.

PREMELLE L.D., containing 0.3mg CEE and 1.5mg MPA, relieves vasomotor symptoms and vaginal atrophy, effectively increases bone mineral density and total bone mineral content, induces favourable changes in lipids, lipoproteins and hemostatic factors, whilst at the same time provides endometrial protection with higher rates of amenorrhoea and no bleeding when compared to commonly prescribed doses (CEE 0.625mg/MPA 2.5mg). In addition, there is no difference in the commonly reported adverse events or changes in mean body weight, although the incidence of breast pain/tenderness appears to be significantly lower, again when compared to commonly prescribed doses of HRT.

A TWO-WAY STREET – THE GYNAECOLOGIST AND THE MENOPAUSAL PATIENT

N Jaff

Since 2002, when the data from the WHI focussed media attention on the increased risks of HT, the relationship between the menopausal woman and her gynaecologist has become increasingly problematic. Many practitioners find that it is difficult to address all the issues of this vast and complex subject in an average 30-minute consultation. The dynamic between the menopausal patient and her gynaecologist has changed and the menopausal woman is no longer the compliant patient, whom the gynaecologist dealt with in her reproductive years. The expectations of this patient are very different. She is older, less tolerant and makes greater demands of the consultation.

The menopausal patient usually arrives at the consultation with preconceived ideas about the menopause gained from casual discussions with friends, the media and the Internet. However, this knowledge often consists of erroneous half-truths leading to confusion and ambiguous feelings about HT. Much of the available information is biased since pharmaceutical and complementary and alternative medicine companies sponsor many of the Internet sites on menopause, and obviously have strong vested interests. The baby-boomers have reached menopause and constitute a significant economic market, which is subject to substantial advertising. Complementary medicines and alternative treatments are advertised in the most attractive way and seem to offer hope of eternal youth and good health to those women who find that they have not been given sufficient attention by their busy gynaecologists. Complementary and alternative medicine practitioners generally spend more time with their patients, and therefore are able to exert disproportionate influence over these women's choice of menopausal treatment.

Menopause is no longer viewed as an estrogen deficiency disease. In general, treating women in menopause has become more complicated because there are both physiological and psychosocial issues to be considered.

Anecdotal evidence from menopausal patients dissatisfied with their gynaecological consultations indicates that women generally feel that they are not given enough information, while that which they are given is often incomprehensible and patronising. They complain that the doctor appears to have his or her own agenda, which they will not modify to suit the specific needs of the individual. The health implications of women's increased longevity are extremely important and the gynaecologist must play an integral role in helping these women enjoy their menopausal years in the best health possible. The consultation should be structured in such a way as to allow the woman to tell her story, to give a medical history, to have a thorough check-up and to understand the risks and benefits of HT. Appropriate laboratory tests, including a mammogram and a DEXA scan, should be mandatory. Technology is not a substitute for good communication. Additional information should be available in the form of a counsellor in the practice, an outside source of information or recommendations of appropriate literature. Communication between the gynaecologist and the menopausal patient is essential to ensure a successful partnership between the two.

FEMALE SEXUAL DYSFUNCTION REVISITED

E L Kok

Department of Urology, School of Medicine, Faculty of Health Sciences, University of Pretoria and Pretoria Academic Hospital, Pretoria

Health care and lifestyle improvements have resulted in many women spending more years in the postmenopausal phase of their lives than in the fertile phase between menarche and menopause. Subsequently quality of life is a real issue for a population of older and generally healthy women.

Postmenopausal women report a relatively high rate of female sexual dysfunction (FSD). Describing sexual function and dysfunction in the menopausal transition is further complicated by new trends and definitions on menopausal stages and women's sexual response.

The primary biological change in menopause is a decrease in circulating estrogen levels. This has a direct effect on sexual functioning through reduced vaginal lubrication and elasticity, resulting in dyspareunia and other urogenital complaints. Hot flushes/night sweats, sleep disturbances and mood changes due to a decline in estrogens can also have an indirect effect

on sexual functioning. A change in female androgen levels, exacerbated by surgical menopause, may also predispose to or precipitate FSD, while the role of progestogens on sexual well being needs further investigation.

Comorbidities exist between mood and desire disorders and urogenital and sexual pain disorders. Both hormonal and nonhormonal factors can influence sexual functioning in peri- and postmenopausal women. Clinical management of FSD should concentrate on measures to promote women's general health, minimalize the sexual side effects of prescribed medication and topical or systemic hormone supplementation with estrogens and/or androgens.

Dealing with FSD in the peri- and postmenopause is a complex issue that calls for a holistic and integrative approach from well trained and committed care givers in the field of women's health.

NEUROLOGICAL AGING – DON'T FORGET TO REMEMBER

Stanley Lipschitz
Rosebank, Johannesburg

There are two cardinal features of aging! Physiological decline and age-dependent disease. Each process may influence the other.

Homeostatic capacity reaches maximum / peak at age 25 to 30 years. From about age 35 years there is a progressive decline in each physiological parameter. A decline below a threshold will result in functional impairment. As a consequence the elderly respond "atypically" to illness presenting with functional impairment (confusion, loss of mobility and independence, falls and incontinence) in response to a variety of illnesses.

Normal aging is accompanied by the sporadic emergence of various forms of pathology.

This presentation will focus on neurological aging. The propensity for the elderly to present with delirium in response to a variety of stimuli will be discussed as will the approach to the assessment and management of this disorder. Failure to manage this disorder rapidly and effectively will inevitably result in further Physical and Cognitive deterioration. An approach to prevention, assessment and management is discussed. Mild Cognitive Impairment (M.C.I) a non-progressive disorder of isolated memory loss differs from Alzheimer's dementia, which is a progressive disorder of global cognitive function associated with behavioral and functional issues. An approach to the assessment of memory disorders will be outlined. Current and future treatment strategies are discussed. Many neurological mechanisms of estrogen action suggest that hormone therapy could beneficially affect the brain in Alzheimer's disease – biological plausibility however does not establish beneficial effect.

BREAST IMAGING

P Oberholzer

The two goals of breast imaging are:

1. **Detect abnormalities**

Mammography remains the gold standard screening tool for breast cancer detection.

70% of DCIS manifests as micro-clacification. Mammography is the most sensitive examination of the detection of mico-calcifications. The sensitivity of a mammogram depends mainly on the density of the breast parenchyma.

2. **Characterize abnormalities** – detected by screening mammography or palpation.

Ultrasound is the examination of choice. It has a far greater ability than mammography to differentiate amongst types of abnormal tissue and to characterize cysts and solid lesions. More specific goals are:

- Initial examination under 35 years
- Guide needle procedures
- Patients with dense breasts
- Stage breast and axilla in the breast cancer patient

MRI

It is the most sensitive examination for the detection of invasive breast cancer. It is a problem-solving tool. Indications are:

- Evaluate the extent of breast cancer especially in labular carcinoma and gives information of the controlateral breat
- Screening of high risk patient (BRCA1/2) with dense breast parenchyma
- Assessment of response with metastatic disease to the axilla and the mammnogram / clinical examination is negative.

CANCER IN THE ELDERLY – IS IT PREVENTABLE?

C Slabber

The number of cancer deaths shows a progressive increase over the past several decades, and is set to overtake cardiovascular disease as the leading cause of death in the developed world within the next 2 decades. This increase is a reflection not only of an aging population, resulting in higher cancer prevalence, but is also due to an increase in incidence of certain malignancies. This has resulted in a doubling in the annual number of cancer deaths in the United States between 1970 and 2000. During this time there was little or no improvement in the mortality rate for the common adult solid tumors. Only in recent years has the mortality for common solid tumors such as breast, lung, and colorectal cancer started to decline. Medical research has focused primarily on the treatment of established malignancies. Impressive results were obtained for a number of cancers in terms of cure rate. This applies to the common adult solid tumors such as breast, colon, and lung cancer when diagnosed *early* and treated with adjuvant chemotherapy. In these cancers the risk of death has been reduced by between 30-50% compared to surgery alone. For the majority of adult patients presenting with *advanced* cancer, improvements in therapy over the past 2 decades have been disappointing. Modest improvements in survival and quality of life can be expected, with improvements in median survival achieved with chemotherapy over the past 3 decades ranging from 1.5 - 3 years for the common solid tumors.

In the developed world, with its aging population, cancer in the elderly presents a particular problem: an unavoidable consequence of aging is the increased risk of cancer. Over 50% of malignancies occur in the 12% of the population over 65 years of age. The development of overt cancer is a complex, multi-step process that occurs over many years in the case of the common adult solid tumors. The elderly are particularly susceptible to the late stages of carcinogenesis due to the physiological consequences of aging, and as a result of carcinogenic mutations collected during their lifetime. Treatment of cancer in the elderly are often associated with specific challenges related to an impaired physiological reserve, co-morbid illnesses, and a limited natural life expectancy.

In the elderly, cancer prevention should be a priority. The best treatment of cancer is its prevention, and that the disease to be prevented is carcinogenesis, not cancer. It is estimated that between 50 – 70% of all human cancers deaths in the developed world are linked to smoking, diet, lack of exercise, or obesity, and can be prevented by lifestyle changes. Additional preventive strategies include screening for the common treatable malignancies, and the use of chemoprevention. Current screening guidelines based on age alone cannot be applied to the elderly, as functional status and life expectancy are important considerations. Chemoprevention appears promising, and efficacy has been demonstrated in a number of studies. Concerns related to tolerance, toxicity, cost, and lack

of long-term safety data has thus far prevented these agents from being use for primary prevention.

A number of factors have limited the efficacy of cancer prevention in the elderly. These factors relate to health care providers and the elderly, as well as the health care system. Cancer prevention in the elderly is feasible, but the success thereof will be determined by the enthusiasm of primary health care providers to implement a cancer prevention strategy, and the willingness of the general population to adopt a healthier lifestyle.

PATHOLOGY AND BIOLOGY OF BREAST CANCER IN POST-MENOPAUSAL WOMEN

Tomas Slavik

Breast carcinoma is the leading cause of cancer death in women worldwide. In South Africa it has become the leading non-dermatological cancer in women. According to the National Cancer Registry (1999), a South African woman has a lifetime risk of 1 in 26 of developing breast cancer, varying from 1 in 49 amongst the black population to 1 in 12 amongst white women.

Although the peak incidence occurs after the menopause, few studies have specifically addressed the pathology and biology of this tumour in post-menopausal and elderly women. According to available literature, mucinous and lobular carcinomas occur more often in this group, which also appears to develop tumours with a more favourable biology. This includes higher expression of steroid receptors and lower expression of HER-2/c-erb B-2 as well as epidermal growth factor receptor.

It was initially thought that breast cancer in elderly women had an exceptionally good prognosis. With improved life expectancy and better treatment of comorbid conditions, more recent studies have shown, however, that the outcome of breast cancer in this group appears to be similar to or even worse than the survival in the general population.

Numerous novel prognostication techniques have been studied in the last decade in an attempt to improve therapy and outcome of breast carcinoma. One of the most promising is gene expression profiling which, although still experimental and relatively costly, appears to be a powerful tool in selecting patients for adjuvant systemic therapy.

HERBAL ALTERNATIVES: DO THEY WORK?

E Sonnendecker

The release of findings from the Women's Health Initiative (WHI) has increased the interest in alternatives to hormone therapy (HT) for treatment of menopausal symptoms. Plant-derived substances structurally related to oestrogens that have been shown to bind to oestrogen receptors, commonly termed phytoestrogens, are currently used by many women as alternatives to HT. Therefore, it is imperative that health care providers are knowledgable concerning the efficacy and safety of commonly utilized botanical preparations. This presentation considers these aspects focusing, albeit not exclusively, on systematic reviews of randomized controlled trials (RCTs).

The main three classes of phytoestrogens are isoflavones, lignans, and coumestans. Isoflavone, in the form of daidzein, genistein and glycetin are found primarily in soybeans. They are the most widely used and studied class. Isoflavones are also found in red clover in the form of biochanin A and formononetin, which are metabolized to genistein and daidzein, respectively after consumption.

Black cohosh (*Cimicifuga* / *Actaea racemosa*) is another plant-derived product marketed for menopausal complaints, which is reviewed. It has unclear mechanisms of action which are not proven to be oestrogenic.

Published studies provide some evidence for positive biological effects but do not conclusively support the effectiveness of these remedies. Nevertheless, they constitute feasible options for symptomatic menopausal women who elect not to use HT or have contraindications. Moreover, phytoestrogens may slow the rate of bone loss but fracture risk reduction remains to be demonstrated. There are concerns about the safety of some botanical preparations and long-term data are largely lacking. More quality evidence is required.

DETERMINING AND ACHIEVING QUALITY OF LIFE GOALS FOR WOMEN AFTER MENOPAUSE

Wulf H Utian

Case Western Reserve University, Cleveland Clinic, and Rapid Medical Research, Cleveland, Ohio, USA

The term "Quality of Life" (QOL) is ubiquitous, and invariably poorly defined. Thus it means different things to different people, both in the scientific world and among women and the general population.

The objectives of this presentation will be to:

1. Make clear the definition of the terms, in particular describing the difference between so-called "health-related quality of life" from "global sense of satisfaction or well-being".
2. Emphasizing the importance of measuring both of these aspects in all areas of medical endeavor, from the research arena to clinical practice.
3. Briefly describing the tools or instruments that can be simply and efficiently incorporated into clinical practice.
4. Itemizing the domains that determine QOL
5. Making recommendations of practical steps for enhancement of personal QOL, which can also be applied in clinical practice. This will be the major focus of this presentation.

Domains of QOL are remarkably consistent through all cultures and socio-economic groups. The major objective of contemporary healthcare should be to assist our patients and populations to achieve these goals. Getting there requires the efforts of multiple public agencies and health care organizations, and the challenge is enormous.

HT AFTER MENOPAUSE – NOW THAT THE DUST HAS SETTLED ON WHI

Wulf H Utian

Case Western Reserve University, Cleveland Clinic, and Rapid Medical Research, Cleveland, Ohio

Over the last few years, I have been privileged to Chair a North American Menopause Society (NAMS) Panel of acknowledged experts in developing Position Statements on estrogen and progestogen usage in peri- and postmenopausal women. The 2004 NAMS Position Statement is accessible with full references at www.menopause.org .

The concept of developing clinical guidelines or position statements is really quite recent, initiated in the 1970s by the U.S. National Institutes of Health with the development of consensus reports. The process changed radically through the 1990s with the "evidence-based medicine" movement that began to mandate a comprehensive and systematic review of the medical and scientific literature and for the requirement that recommendations needed to be directly linked to supporting evidence. NAMS commenced development of consensus opinions in 1998, emphasizing that they do not represent "practice standards" that would be codified and held up as standards by regulatory bodies and insurance agencies. Rather these are prevailing opinion pieces, attempting a best effort at incorporating current best evidence into practical clinical recommendations.

The NAMS HT positions together with those of other significant organizations will be presented with practical application to contemporary clinical practice. Where appropriate, key factors from the published literature will be presented to substantiate an appropriate position.

Translating these positions into clinical practice necessitates taking into account the complete health profile of the individual woman as well as her personal preferences and beliefs. The purpose of Position Statements is intended to enhance the quality of patient care and to modulate the clinician's pattern of practice. Evidence based review of the literature has enabled placing of the WHI results in perspective of the big picture and clarified the appropriate standards of current practice. These recommendations will be the main purpose of this presentation.

INSULIN RESISTANCE – WHAT DOES IT MEAN AND WHAT TO DO ABOUT IT?

Zephne M van der Spuy

Department of Obstetrics and Gynaecology, University of Cape Town

The polycystic ovary syndrome (PCOS) is the commonest endocrinopathy in women of reproductive years. The impact of this condition includes reproductive dysfunction and metabolic disturbances. While previously the investigation and management of these patients focused on their reproductive needs, it is now recognized that the long-term impact of the condition may result in an increased prevalence of diabetes mellitus, dyslipidaemia and coronary artery disease in later life.

Obesity and abdominal obesity are common in PCOS and studies from different units report varying prevalences. It is commonly accepted that a BMI outside the acceptable normal range, and often in the overweight range, is common in patients with PCOS. Increased BMI and particularly abdominal obesity worsens the clinical features of PCOS and impacts significantly on the endocrinopathy. Insulin resistance correlates with obesity and may be the key metabolic defect in the aetiology and development of PCOS. Several mechanisms of action have been proposed including impaired insulin-stimulated glucose uptake and suppression of lipolysis in the muscles and adipose tissue, hepatic glucose over-production and suppression of glycogen synthesis. Obesity, particularly central obesity, impact strongly on the development of insulin resistance in women both with and without PCOS. This obviously will have a long-term impact on their health and may result in increased morbidity in later years.

Hyperandrogenism correlates positively with insulin resistance in women with PCOS, both in those who are obese and those of normal BMI. This impacts on the disease presentation, the endocrinological abnormalities and the ultimate management of these patients. The diagnosis of insulin resistance may be difficult but in clinical practice utilizing a glucose-insulin ratio is helpful in the management of these patients.

There has been considerable discussion and controversy on the best dietary advice which should be given to patients and diets which have been designed for women with PCOS and insulin resistance vary considerably. Essentially there is considerable support for a diet with a reduced glycaemic index but good data from RCTs is presently not available. Life-style changes are very important in the management of these patients but obviously are extremely difficult to implement.

Of major concern are the long-term consequences of PCOS. These include metabolic, cardiovascular and neoplastic risks. The metabolic abnormalities are particularly concerning and may result in an increased prevalence of diabetes mellitus, cardiovascular disease and dyslipidaemia. The metabolic syndrome has been defined as a condition which includes increased fasting triglycerides, high HDL cholesterol, blood pressure measurements exceeding or equal to 130/90 mmHg, serum glucose more than 6 mmol/l or waist circumference exceeding 88 cm. This syndrome occurs in about 46% of women with PCOS which is almost double the prevalence in the normal population. The multiple risk factors for cardiovascular disease include dyslipidaemia, hyperinsulinaemia and hypertension. The risk factors for malignancy are less well defined and impact on endometrial carcinoma in patients who are inappropriately managed.

Clinicians need to identify cardiovascular and metabolic risk factors in women with PCOS at a young age. Therapy must aim at the management of these patients over decades and not concentrate solely on their fertility requirements. Family studies are important and appropriate counselling must be given to siblings and daughters of women with PCOS. Ultimately therapy concentrates on the particular clinical problem, the long-term consequences of the condition and the management into the menopause and beyond.

CARDIOVASCULAR DISEASE IN WOMEN

CJ van Wyk

Women worry more about breast cancer than heart disease, yet cardiovascular disease is the leading cause of death in women and is responsible for more deaths than all other causes combined. This risk increases dramatically after menopause.

With coronary heart disease it is found that the mortality in women is higher compared to men. This is largely due to the co-morbidities of increased age, diabetes mellitus, hypertension etc., as well as the under utilization of treatment strategies both pharmacological and re-vascularization.

HOW TO REKINDLE YOUR SEX LIFE AFTER 50

M Wasserman

Female sexual function changes significantly in midlife. International scientific studies indicate that coital rate decreases with age and the length of the relationship, sexual activity declines and that there is a sharp decline in sexual interest in women over 50. In addition there is a decline in enjoyment , arousal and orgasms. Physical health problems, loss of a partner, lack of partner availability , partner's health and medication usage contribute to this increase in Female Sexual Disorder (FSD) in peri and post menopausal women.

Psychosocial stressors equally contribute to neatly putting aging women's sexuality to bed.

In this paper the epidemiology of FSD in aging women will be presented. Attention will then be turned to a multidimensional view of the impact of aging on sexual function and satisfaction. Understanding the tremendous impact and influence of sex hormone, particularly estrogen and testosterone, on women's sexuality at menopause is vital to good management. However the psychosocial aspects of menopause on sexuality have to be considered and given equal weight during assessment and management.

The controversial issue of HRT, including testosterone, use will be discussed within the context of the sexuality of an aging woman.

Intimacy remains the driving force in women's sexual satisfaction. Rekindling her sex life after 50 requires health care providers to give this aspect of her life attention, not just focus on the biological and hormonal aspects of aging. Substantive ideas and recommendations on how to enhance her sexuality will be presented. Wet cloths and fans will be provided to each participant to dampen the hot flashes this will create during discussion!