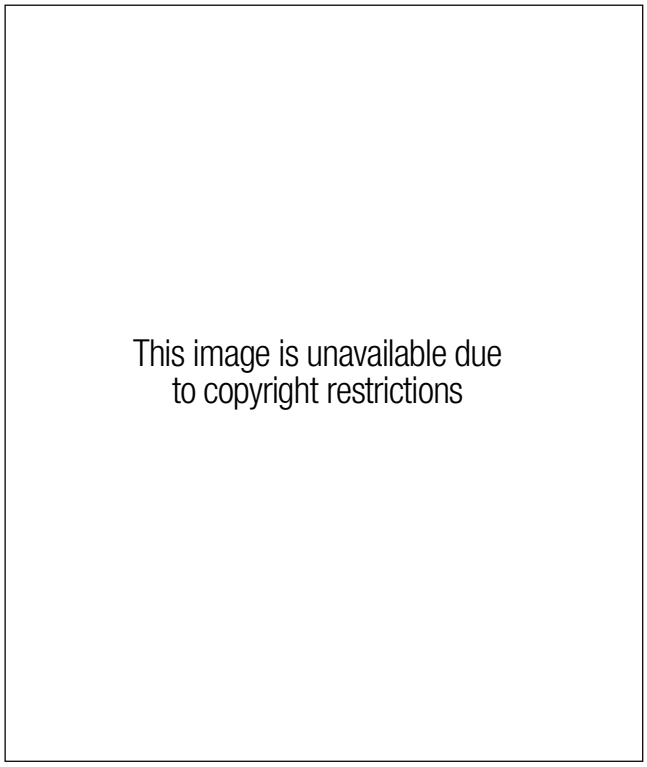
The use and abuse of screening tests around menopause

ALASTAIR H. MACLENNAN MB ChB, MD, FRCOG, FRANZCOG
DAVID W. STURDEE MB ChB, MD, FRCOG

'Listen carefully to the patient, take a good history and examine her. Then you will need few, if any, diagnostic tests to determine the correct diagnosis and treatment.' 'Don't order a test if it is not going to change your management.' 'Unnecessary tests create unnecessary costs, unnecessary anxiety and sometimes unnecessary interventions.' These old adages are still true, particularly when a woman presents around menopause with typical menopausal symptoms. Nevertheless, many otherwise healthy women are referred to menopause clinics by doctors who are unsure of the management of the menopause, with a battery of negative screening tests performed at great expense to her, her insurers or the national health system. Commonly, the woman arrives with a thick file of tests showing normal haematological counts, renal and liver function tests, electrolytes, cholesterol, thyroid function and urine analyses. Expensive hormone tests often inexplicably include unnecessary progesterone, luteinising hormone and dehydroepiandrosterone levels and include predictably high follicle stimulating hormone (FSH) and low oestrogen and testosterone levels. The value of screening the menopausal population with these tests remains controversial, unproven and is often a waste of resources. Of course, in women with relevant risk factors, symptoms or signs, it is appropriate to order a lipid profile, random blood sugar, complete blood picture or thyroid function test, which may change management.

The value of screening for hypothyroidism may vary around the world where local incidences are high. Cost efficiency increases in the elderly. However, there is no need for an indiscriminate battery of tests to be part of the work-up of a normal postmenopausal woman before she can be offered oestrogen and progestogen therapy. Nearly all symptomatic women over the age of 50 years have high FSH and low oestrogen levels.

Professor MacLennan is Head of Discipline of Obstetrics and Gynaecology, School of Paediatrics and Reproductive Health, The University of Adelaide at The Women's and Children's Hospital, North Adelaide, SA.
Dr Sturdee is a Consultant Gynaecologist at the Department of Obstetrics and Gynaecology, Solihull Hospital, UK; and is President Elect of the International Menopause Society.
This article was originally published in Climacteric (2006; 9: 153-155) and is reprinted here with permission.



ISTOCKPHOTO

Perimenopause oestrogen levels fluctuate daily, making them of little diagnostic or therapeutic value, and FSH and oestrogen levels are not helpful to titrate or juggle hormone therapies. However, women often expect hormonal testing at the menopause and are unaware that these tests are usually unnecessary and may be inaccurate, leading sometimes to inappropriate non-treatment despite the presence of debilitating menopausal symptoms at the perimenopause. Recently, nonevidence-based entrepreneurial pathology laboratories have exploited public naivety about the clinical usefulness of hormone tests. They have touted nonsense salivary hormonal testing directly to a gullible public via internet advertising or through practitioners and compounding pharmacies that benefit from selling so-called bioidentical or bioequivalent hormones supposedly tailored to the salivary results.[1]

A high serum FSH level can be helpful to confirm a premature menopause, a high testosterone level in women with hirsutism may suggest possible ovarian pathology and a very high oestrogen level can confirm tachyphylaxis after excessive use of oestrogen implants. Other than in these uncommon situations, hormone testing rarely changes management. A simple menopausal symptom score chart, such as in Table 1, at no cost can help to grade probable oestrogen deficiency symptoms.[2] It can be used by both doctor and patient to monitor response to hormone therapy. Patients score 0 to 3 (none, mild, moderate or severe) for the presence of 20 symptoms grouped as vasomotor, psychological, locomotor and urogenital symptoms. Scores of 20 to 50 out of a

continued

Table 1. Menopause symptom score

In the last week, for any reason, have you had any of the symptoms listed below? Score 0 if none, 1 if mild, 2 if moderate, and 3 if severe).

Oestrogen deficiency symptoms	Before hormone therapy	Three months after starting	Six months after starting
Hot flushes			
Light-headed feelings			
Headaches			
Irritability			
Depression			
Unloved feelings			
Anxiety			
Mood changes			
Sleeplessness			
Unusual tiredness			
Backache			
Joint pains			
Muscle pains			
New facial hair			
Dry skin			
Crawling feelings under skin			
Fewer sexual feelings			
Dry vagina			
Uncomfortable intercourse			
Urinary frequency			
Total score			

possible 60 are common in symptomatic women before therapy and successful treatment usually brings the symptom score down to around 10 within three months.

Fear of breast cancer is still a dominant concern of both menopausal women and their prescribing doctors. Routine mammographic screening is widely recommended for menopausal women, but there is no merit in additional screening prior to or during hormone therapy.

Screening of all menopausal women for risk of osteoporotic fractures is also controversial and currently not advocated.[3] However, selection of at-risk women for bone density testing, in which the result may influence current or future management, is a reasonable policy. Future population screening for fracture risk will depend on many factors, including improved prediction of fracture risk, low cost of screening, general availability of screening and, not least, an effective, safe and low-cost intervention to be introduced at an intervention point defined by the screening in which low numbers of women need to be treated to prevent one fracture. Currently, the bisphosphonates and selective oestrogen receptor modulators have difficulty reaching these criteria before a fracture has occurred. The recent reanalyses of risk for oestrogen, especially low-dose and unopposed, therapy and the therapeutic window of possible cardio- and neuroprotection for hormone therapies around menopause have recalculated the risk–benefit ratio for the treatment of osteopenia and osteoporosis in younger postmenopausal women and could influence the greater use of bone density testing in this group.[4]

The increasing technical ease of screening for genetic polymorphisms is one of the next great challenges for medicine. The ability to measure cheaply such mutations in blood or other tissues is quickly outstripping the knowledge of the clinical relevance of these genetic markers and whether clinical interventions are necessary or cost effective in those who are heterozygous or homozygous for these polymorphisms. Within a couple of years, it is likely that entrepreneurial pathology laboratories will market directly to the public the opportunity to have their genetic profile checked for a variety of mutations that increase the risk of specific diseases. It will probably be possible for practitioners to test for specific mutations with microtechnology in their consulting rooms. Predictions of increased risk of cancer (e.g. breast), cardiovascular disease and dementia will all be possible. Already, we know that many of those who experienced

thromboembolism on hormone therapies in some of the major randomised controlled trials had a Factor V Leiden mutation.[5,6] Is it worth screening for this mutation, which is present in about 5% of the US population and 10% of the Caucasian Australian population? How do the risks vary between the homozygous and heterozygous variants? Can oestrogen be prescribed to these women with or without anticoagulation? Answers to such questions and an understanding about the clinical utility and adverse consequences of genetic screening are needed before they are commercialised and abused.

The explanation and understanding of clinical risk suggested by genetic mutations is a difficult task. Such screening could also precipitate unnecessary interventions. Individuals could claim that they were not counselled before screening about the ramifications of genetic screening, which could include employment discrimination and exclusion from health insurance. Screening for genetic polymorphisms before there are adequate answers to these medical, social and legal problems will create many problems and not least may engender great anxiety amongst those who have paid the modern fortune-teller to look into their genes. For the moment, this is a genie or geneticist that should be kept in the bottle! MT

References

1. MacLennan AH, Sturdee DW. The 'bioidentical/bioequivalent' hormone scam. Climacteric 2006; 9: 1-3.
2. MacLennan AH, MacLennan A, O'Neill S, Kirkgard Y, Wenzel S, Chambers HM. Oestrogen and cyclical progestogen in postmenopausal hormone replacement therapy. Med J Aust 1992; 157: 167-170.
3. Torgerson DJ, Donaldson C, Reid DM. Bone mineral density measurements: are they worth while? J R Soc Med 1996; 89: 457-461.
4. Stevenson JC. Justification for the use of HRT in the long-term prevention of osteoporosis. Maturitas 2005; 51: 113-126.
5. Cushman M, Kuller LH, Prentice R, et al. for the Women's Health Investigators. Estrogen plus progestin and risk of venous thrombosis. JAMA 2004; 292: 1573-1580.
6. Herrington DM, Vittinghoff E, Howard TD, et al. Factor V Leiden, hormone replacement therapy, and risk of venous thromboembolic events in women with coronary disease. Arterioscler Thromb Vasc Biol 2002; 22: 879-880.
7. Gibson CS, MacLennan AH, Rudzki Z, et al. The prevalence of inherited thrombophilias in a Caucasian Australian population. Pathology 2005; 37: 160-163.
8. MacLennan AH, Sturdee DW. The use and abuse of screening tests around menopause. Climacteric 2006; 9: 153-155.

Acknowledgements

This article was originally published in Climacteric (2006; 9: 153-155) and is reprinted here with permission.