INVITED SUBMISSION TO NHMRC WORKING PARTY ON HORMONE REPLACEMENT THERAPY FOR PERI AND POST MENOPAUSAL WOMEN- 29 September 1995.

AUTHOR : Shelley L. Beer (Research student-PhD medicine) Department of Public Health and Community Medicine, University of Melbourne. Senior Lecturer , Department of Health Sciences, Victoria University of Technology

Hormone Replacement Therapy & Alternative Medicines 1: 1936-1995

Introduction

In 1995, the National Health and Medical Research Council (NHMRC) directed a working party to report on Hormone Replacement Therapy (HRT) in peri- and post menopausal women. The terms of reference sought to compare HRT's performance compared to alternative therapy options. With very little *comparative* research done in this area, the information presented in this submission evaluated the literature documented for alternatives to hormone therapy in the perimenopause and post menopause to that time.

Overall, the nature of research to 1995 that had been done is limited to evaluating individual approaches, without reference to HRT. Such studies include the use of Vitamin E, Evening Primrose Oil, extracts of *Cimicifuga racemosa*, soy protein supplements and the use of Chinese herbal medicine as practiced in Japan.

In Australia, the first double-blind placebo-controlled trial of Chinese herbal medicine to be ever tested had been underway since ethics approval on 16 March 1994, but the trial was still recruiting participants, so no result could be reported here. The author has located only one study that evaluates hormone therapy and Chinese Herbal medicine in the same trial. Although it is not a comparative trial, its conclusions provide persuasive recommendations that the NHMRC Working Party could consider for action. (Mochimaru *et al.* 1984) recommended herbal medicines in natural menopause, and estrogens for surgical menopause.

This paper will examine the detail of the state of research to 1975 in the alternative therapies field with regard to hormone therapy alternatives. This field does not enjoy the large financial support that western medicine attracts. Although it is hypothesised anecdotally (Swan, 1994) that Natural therapists are not willing to test their products, this author has experienced more a lack of funding and very limited support for alternative research from within the orthodoxy that explains the lack of data.

For example, the Australian study referred to above (Beer, 1995, unpublished data) took four years for approval through the University of Melbourne ethics processes. In addition, fear that Chinese herbs had not previously been tested in a research setting led to conditions being set by this author's own department for a medical practitioner to be involved in the study. In a department that is made up principally of doctors, none were available to fulfill this condition. An external medical practitioner had to be recruited, yet there were no funds available to employ this person. The study was almost stopped before it had begun. An anonymous donor for the gynaecologist's contribution to the study was found at the "eleventh hour" and so the trial was finally able to commence. These types of obstacles serve to limit the production of research in alternative medicines. Herb companies are not the powerful economic force that drug companies appear to be and so independent research has been relatively limited.

At the time of writing, this author saw potential for change to the above factors, as the public was actively seeing alternatives. In addition, the pool of potential researchers would grow as Australian Universities produced Bachelor degree graduates in Acupuncture (Victoria University of Technology, University of Technology, Sydney) and Natural therapies (Southern Cross University). Post-graduate programs were commencing or under way in Acupuncture, Chinese herbal medicine

and Western herbal medicine (Victoria University of Technology). The natural flow on of research students into these areas would see more data produced in the fields of alternative therapies.

Thus, the lack of data with regard to HRT comparisons and alternative therapies in 1975 need not be interpreted as definitive proof that limited research means there was no scope for evaluation of alternatives. As with any research, the lack of volume in research may not be proof that there is no benefit. It just means that little research had been done. The little published results that existed were enough to be considered pilot studies for future research and hence potential action/recommendation for the NHMRC Working party.

The Climacteric

The climacteric is the time period which leads up to the menopause - the cessation of menstrual bleeding. Menopausal issues have become the focus of research in recent years. Poor methodology has seen the conflation of physiological, socio-cultural and life-span change factors into one causative agent: for any distress which has arisen at this time (Kaufert *et al.* 1988). Based on clinical samples, retrospective reporting and cultural stereo-types, the conclusion that oestrogen has been at the root of all problems facing the climacteric woman has been a reasonable conclusion - for the evidence generated.

Physiological VS Social Factors

More rigorous methodology has determined that *only* vasomotor disturbances can be directly attributable to the physiology of the climacteric and menopause itself (Utian 1972). Conversely, it is inappropriate to relegate any other problem that arises at the same time, as caused by lack of circulating oestrogens (Morse 1989). Emotional responses to physiological discomfort, changed life roles and cultural expectations have been largely socially constructed (Hunter 1990). This viewpoint now emphasises that estrogen supplementation has no role to play in the treatment of depression at the climacteric (Ballinger 1985), although sleep can benefit when estrogen is applied for vasomotor disturbance which can contribute to insomnia.

Hot flushes and hormone therapy

The significance of the climacteric for individual women varies. If vasomotor disturbance (hot flushes) is predominantly a problem, Hormone Replacement Therapy (HRT) works well (Kronnenberg 1990). However, it has been applied widely not only because it appears to be the most effective agent - but also because in 1975, it *appeared to be* prophylactic for a number of longer-term problems of aging: vaginal atrophy, osteoporosis and cardiovascular disease. Prophylaxis has been based on epidemiological research, and not on long term, controlled studies, so it is wise to examine the evidence that might support such strategies.

Cardiovascular disease and Hormone therapy

With regard to Cardiovascular disease (CVD), there is a disturbing trend that advocates women should be using hormone therapy because coronary heart disease (CDH) is the biggest killer of white women over 50 years of age (Cummings, Black and Rubin 1989) and hormone therapy is claimed to decrease the risk of death from CHD by 50 % (Cowan *et al* 1987, Barrett- Connor & Bush 1991, Stampfer 1991). These figures are derived from epidemiological survey, and not from controlled trials. Until long-term trials are complete, this evidence remains speculative. However, with a mean age death from CHD occurring around 74 years (Grady, Rubin, Petitti *et al* 1992) one must be careful in analysing statistics in this area. Goble (1992) raises the question whether certified deaths can be taken to be reliable, and concludes that at 75 years, certification is only "possibly accurate' (p13).

Is CHD the biggest killer of women over 50, or is there some other cause? Goss, Neufeld, Libow *et al* (1988) evaluated 234 cases that were originally certified as death caused by ischemic heart disease. Autopsy revealed that "If one included congestive heart failure from all causes, myocardial infarction and cerebrovascular accidents together, they accounted for only 28 % of primary causes of death as determined by autopsy" (Goble 1992: 12) Pneumonia caused 33 % of deaths, cancer caused 14 % and pulmonary embolism 8 %. This evidence is offered to explain the alarmingly high rate of death by natural causes being certified automatically as CHD. Although women targeted for HRT as prophylaxis are not by and large the very elderly, the very elderly are contributing to the figures that are used to justify /analysise risk factors.

Relative risks and Benefits of HRT

Not all women can take estrogens without adverse effect on existing illness (Llewellyn-Jones 1986). Oestrogen therapy by itself has been implicated in breast cancer (Thomas 1984, Colditz *et al.* 1990) and endometrial cancer (Antunes *et al.*1979). The need to oppose oestrogen with progestogens to reduce the risks of oestrogens taken alone, then reintroduces cyclical bleeding and may cause general metabolic disturbances that can be distressing (von Eikstedt and Lang 1989, Smith, Holland & Studd 1994). Others may welcome the improved libido which this combination can induce (Dennerstein 1978).

A 50 year old white woman has the following chances of developing degenerative illness during the rest of her life time - CHD 46 %, Stroke 20 %, Breast cancer 10 %, Endometrial cancer 2-3%, Hip fracture 15-16%. Her chances of dying from these illnesses are estimated to be - CHD 31 %, Stroke 8%, Breast cancer 3 %, Endometrial cancer 0.3 % Hip fracture 1-3 %

Long term use of HRT has been estimated to decrease the risk of coronary heart disease by 33 % (Cummings, 1991) to (RR 0.7), yet without a randomised trail Cummings "cannot be completely certain that estrogen therapy reduces the risk of Coronary heart disease "(1991: 10). There appears to be little impact on stroke. Estrogen is known to increase the risk (RR 1.3) of breast cancer by 25 % over 8 years (1991: 11) and increases the risk (RR 8.2) of endometrial cancer an alarmingly high rate to approximately 24%. Although estrogen alone increases the risk of cancer, it appears that the type of cancer is a lower grade, and so the risk of death from endometrial cancer is lower than the risk of developing the cancer. It is commonly accepted that by adding a progestin to the regime, the risk to a woman returns to normal levels of risk. (Cummings 1991: 11)

As researchers investigate the long term effects and risk factors of HRT use, opinion about its use is becoming divided.

Is estrogen the answer? Are the right questions being asked?

Because of the doubts expressed as to safety of HRT, there has been a move to delve further into a woman's endocrinological factors to determine a more precise mechanism for the origin of the hot flush. According to several writers, estrogen withdrawal is not the instigator of the hot flush. Rather, the hot flush is considered to be a specific disturbance of menopausal women's thermoregulatory centres, with reduction in estrogen levels only being a coincidental change (Taltaryn *et al.* 1980, Linsell & Lightman 1983).

Sturdee *et al.* (1978) showed that the onset of the hot flush is associated with a sudden and transient increase in sympathetic drive. They suggested that an improved understanding of the changes that occur in association with hot flushes will lead to a more specific alternative to estrogen to relieve the symptoms (Sturdee et al. 1978). If lowered circulating oestrogens aren't the *cause*, but an observed concomitant change in hormone profiles, then perhaps replacing oestogen is not the most appropriate method for supplementation.

Other drug treatments

Investigations to replace oestrogen with other drugs have revealed contradictory results. Clonidine, an alpha-adrenergic agonist that reduces responsiveness to exogenous vasoactive amines has been proposed as a suitable, effective drug to treat menopausal flushes by some (Clayden *et al.* 1974) while other studies have shown that it is ineffective (Wren & Brown 1986). Treatments by

substances which decrease pulsatile release of Luteinising Hormone (LH) also reduce the frequency of flushes (Lightman *et al.* 1981). These substances [Medroxyprogesterone, Naloxone] although clinically useful, are not considered as effective as HRT.

What do women want? Who determines need?

Women themselves are expressing dissatisfaction with pharmaceutical drugs as a way of dealing with disturbing menopausal symptoms (Voda & Eliasson 1983). Researchers too are starting to question the wisdom of long tern HRT use. In 1991, S.R. Cummings opened the XIIIth World congress of Gynaecology and Obstetrics with a paper acknowledging that physician's priorities and women's priorities "generally differ" (Cummings, 1991: 12). As a result, he felt that women should set their own priorities, after they have been informed of all risks and benefits associated with long term hormonal use. A 1992 review of the literature concluded similarly- for the majority of women, "the best course of action is unclear" (Grady *et al* 1992: 1016). It is timely to investigate an alternative non-synthetic agent that may treat the menopausal vasomotor disturbance.

Self-help- myth or an actual strategy?

Although work has been done in a number of natural therapy areas, mention is made here only for the purpose of acknowledgement. Vitamin E has been considered by many women to be a favourable home remedy for hot flushes, along with evening primrose oil. Although Blatt, Weisbader and Kupperman (1953) determined that Vitamin E was ineffective, their menopausal index has since been criticised for not being a true indicator of menopausal status . More recent evaluation has included Vitamin E conjugated with Evening Primrose Oil (Chenoy, Hussain, Tayob *et al* 1994). Although night time flushes improved, the authors considered that gammolenic acid offers no benefit over placebo for daytime flushing. As women who called this author between 1994 & 97 continued to report that they had been using Vitamin E and Evening Primrose Oil as self therapy with little effect, studies in this area would need to mimic the naturopathic protocols that prescribe these supplements. This author recommended that the committee examine submissions from practitioners who specialise in those areas who are able to comment on the relative strengths or weaknesses of previous studies. Were therapeutic doses being tested for example? Pervasive belief by the population in these substances warrants definite trails that are convincing.

Recent work on an extract of an orthodox herbal medicine: *Cimicifuga racemosa* has been demonstrated to selectively suppress LH secretion in menopausal women (status not described, symptoms not measured) according to blood assays (Düker *et al.* 1991) performed on ovariectomised rats and menopausal women. Its effectiveness had not been demonstrated clinically, yet it commenced being sold over the counter in Australian chemist shops as *Remifemin*. As its action is more like *Naloxone* and *Medroxyprogesterone* (above), its strength appears to be not as effective as HRT with regard to flushing.

Phytoestrogens

Phytoestrogens have been gaining prominence in the literature. It is noted that menopausal symptoms rarely occur in cultures that are oriental (Haines, Chung & Leung 1994). It is noted also that these culture's diets are high in soy protein or plants are used at home as herbal medicines/ soups (Lock 1986). At high levels, plants containing either isoflavones, phytoestrols, saponins or lignans are capable of exerting estrogenic effects that are significant (Kaldas & Hughes 1989). Foods and herbal medicines which have been identified to have estrogenic activity, such as wheat and soy products (Murkies, Lombard, Strauss *et al* 1995) have been shown to decrease hot flushing experiences by 40%. Although placebo effect confounded the results (no controls), the results suggested a simple strategy for women with mild flushing. Encouraging phytoestrogen animal studies have not been shown to cause the prothombotic effects that estrogens pose. They even appear to inhibit mammary tumors (Rose 1992). More studies in this area would seem warranted.

Although many Chinese herbal medicines have been identified to contain estrogenic precursors, such as ginseng and Chinese angelica (Chang & But 1987) the main self- administered tonics in the pharmacopoeia, their use is not prescribed according to western physiological principles.

Chinese Medicine and the Climacteric

Traditional Chinese Medicine (TCM) has been used in a systematic format as recorded text since approximately 100 BC. An empirical medicine system, it has constantly evolved, retaining that which is useful, whilst discarding ineffective or dangerous practices. It applies treatment according to the principle of *Bian Zheng Lun Zhi* (BZLZ). This means that one Western -named disease is not treated with the same substance in all women. Syndromes (Clustering of symptom patterns) are classified into many patterns of dysharmony, just as one pattern of dysharmony may be expressed by many Western-named pathological disease states. TCM takes account of the presenting symptomatic profile of the **entire** person as they relate to their environment, social situations and their personal emotional responses to these. Each individual pattern is treated according to the differential diagnosis based on this principle. There is not one formula for "Climacteric Syndrome", but a number of formulas to be discriminated between, according to the individual's TCM diagnosis. The routine application of a single agent to treat an isolated symptom for any woman ignores the level of discrimination that is required to safely administer herbal drug agents. As such, it is inappropriate to apply a single formula to an entire cohort of women. Even more inappropriate is the trend to discover isolated active constituents with the intention of applying the individual constituent to all women without the balancing checks of the co-existing naturally occurring constituents. The purpose of pharmacognosy is served at the point of identifying toxicity levels, and appropriate therapeutic doses.

Cultural mores demonstrate that Chinese women don't present at the climacteric for treatment of hot flushes (Tang 1991). The physiology of oriental peoples may be a contributing factor (Kuno 1959, Lock *et al.* 1988), as may be the differing sociological values that apply to women in a culture that revered aging and valued continuing family ties.

Traditional Chinese Medicine's use in Japan is known as Kampo Medicine. In modern times, the Kampo application of TCM has seen the marriage of Western scientific investigation while retaining some of the traditional indications.

Research & Traditional Medicines

1.China. The TCM literature does not focus on the menopause as a disease entity. Interest by the West has necessitated analysis by TCM theory to describe such a presentation. Thus, most literature remains a theoretical description of how a practitioner may choose a suitable treatment (e.g. Dharmanda 1988).

Research in the Peoples Republic of China had therefore mainly focused on the chemistry of plant materials, with insufficient attention having been paid to the interpretation of the pharmacological mechanisms. Deficiencies in this type of work particularly are that it isolates active constituents from the whole effect of a compound formula. There are observed differences between the known effect of the active constituent parts of a formula and the combined formula's ability to exert a therapeutic effect (Xu *et al.* 1985). Yet there is also demonstrated research that confirms herbal theoretical effect, consistent with the pharmacological action (Shibata 1970).

Toxicological studies of individual herbs have been documented widely. These have ranged from clinical reports of inappropriate dosages, pharmacological studies and laboratory testing of LD 50 determinations in a variety of animals (e.g. Takagi & Shibata 1969, also see Chang & But 1986, 1987). Although there is much work needed to demonstrate the clinical efficacy of herbal medicines, the volume of Phyto therapeutic research suggests that "efficacy and safety" are being demonstrated at this level (Xiao & Chen 1987: 61).

2. Japan. Research has principally focused on the endocrinological application of isolated active constituents, or clinical evaluation of many different formulas with little attention paid to controls. In laboratory animals it has been demonstrated that many TCM formulas have normative effects on ovarian function (Koyama *et al.* 1988), but not specifically for menopausal women. Clinical case reports are very common and as such lack sufficient rigor to be considered conclusive, despite conclusions claiming that they are "effective"(e.g. Akiraco *et al.* 1979). There is also the tendency to combine theoretical proscriptive recommendations with illustrated case histories (Ishino 1992). The most commonly cited indications for Kampo medicines are for "Climacteric syndrome and ovarian deficiency" (Igarashi 1988: 142). In a culture which accepts the marriage of herbal medicine within its Gynaecology clinics (66.9 % of gynaecologists in Japan [2479 surveyed] use Kampo preparations), it is understandable that less attention has been paid to controlled trials. There is no need to prove that which is already known. The benefit that can be derived from the research in Japan is that it offers strong evidence for clinical trials to be conducted in Australia.

Traditional Medicines for Climacteric Disorders

a) Therapeutic Principle

TCM theory describes the climacteric as a natural progression of aging, in accordance with TCM physiology. Natural aging theory most closely fits the TCM pattern of dysharmony known as "*Kidney* and *Liver yin* weakness with *xu fire (empty fire)* flaring upwards" This pattern includes such presenting symptoms as hot flushes, night sweats with fever, irritability, insomnia and thirst. Although this list resembles vasomotor disturbance of western medicine, the list alone is not the key to prescribing. It is the cause of these symptoms, and not the symptoms themselves which will determine the treatment principle. Treatment of this pattern employs herbs to nourish the *Kidney & Liver yin* and to bring down the weak fire.

Since there endures a view of severe climacteric symptoms as a disease state, the term "Climacteric Syndrome" is used in the USA and Japan to describe women who are not coping with the changes taking place in their bodies. Distressing symptoms do require attention. In women who present with distress, their TCM diagnosis more commonly describes the "declining *liver blood* becomes stagnant and generates heat which flares upward". The Kampo formula of choice most commonly cited in the Japanese literature for this presentation, is **"Bupleurum & Peony Formula"**, called **"Kamishoyo San"** or **"TJ-24"** in Japan (e.g. Mitani 1992, Ishino 1992). The TCM literature indicates that this formula would not address the long term need for nourishment of the declining *blood* but in the short term is considered suitable for Caucasian women (Dharmananda 1988) if the correct syndrome applies. Follow up treatment requires that the principle of nourishing the *Kidney & Liver yin* would be paramount.

b) Clinical Application

Despite the literature describing over 10 main categories for "menopausal syndrome" (Flaws, 1992), each textbook pattern is not exclusively seen in clinical practice. A number of patterns may be intermingled. Additionally, these 10 categories may be further differentiated for each individual woman from a base of approximately 36 different guiding formulae. There are 13 typical syndromes named in the literature (Flaws, 1992, Wolfe, 1993) with 36 guiding formulae. This does not take account the process of "Jia Zhen" - addition/subtraction for tailoring individual prescriptions (Flaws, 1993). 'Clearly, it is imperative that a detailed TCM diagnosis is made by someone trained in TCM, as the possible variation in choice is as varied as the woman who presents with troubling symptoms.

The University of Melbourne Department of Community Medicine Ethics committee was not open to the above information and made a condition of going forward, that one formula was to be tested using a placebo, random, double blind trial. In addition, the formula to be tested was required to have already undergone research elsewhere, because a Chinese Herbal medicine trail had not been done in the Faculty of Medicine at that time.

¹ Detailed analysis of these are the subject of another paper which will follow in this series

There was textbook reporting of a formula developed by a Shang Hai Hospital for hot flushes (Two Immortal Powders), but its use was not listed in Australia according to Therapeutic Goods regulations in 1975. For formulas also listed with the TGA, one had to look to Japan for research trial.

Kampo Medicine uses a combination of Western Scientific Medicine, yet retains the TCM principle of "Bian Zheng Lun Zhi." (Mochimaru *et al.* 1984). Mochimaru *et al.* applied the use of a Terumo thermistor probe (Meldrum *et al.* 1979) to demonstrate certain correlations between the experience of flushing, the suitability of Premarin, Kampo formulas, tranquilisers or the suitability of counseling for the treatment of Post-menopausal hot flushes. As the only descriptors used were 3 degrees of improvement, and a measured decrease in skin temperature, the results cannot be considered conclusive. The degree of effectiveness for flushes alone was not clearly delineated for the Kampo drugs, although they were recommended "as a first choice if hot flashes result from natural menopause" (Mochimaru *et al.* 1984: 644). That study recommended the use of premarin for cases of surgical menopause.

Another study also looked at post-menopausal women in a number of Kampo formulas. Bupleurum & Peony is called "Kamishoyo-san" in Japan. It was demonstrated to be 93.3% effective, yet it was not possible to determine if this was for hot flushes alone; as the outdated Kupperman ²Index was the main measure of subjective improvement (Kano *et al.* 1985b). To a lesser degree, a change in hormone profile according to E2, LH, FSH and progesterone levels was considered a marker of improvement. In a group of 28 women, menopausal status unknown, between 38-61 years "Kamishoyo-san" was declared effective against "difficulty in falling asleep, light sleep, excitability, nervousness, depressed mood, hot flash, sweating and palpitation" (Kano *et al* 1985b: 214). Again, it is difficult to rely on the results, as the Kupperman Index was the only measure used that showed a change. It was demonstrated that that even though the Kampo drugs were effective in conjugated estrogen -resistant menopausal women, the blood levels of FSH, LH and estradiol were not significantly changed.

The overall trend for Kampo medicine to exert an effect has been hypothesised by one study to effective on the hypothamic- pituritary -ovarian axis. In pre-menopausal women this has been shown to bring about bleeding in amneorrheic women, ovulation, luteal phase normalcy and / or pregnancy (Koyama *et al* 1988). Results which report blood assays, such as this one and the one by Kano *et al* (1985b) cannot be considered placebo.

Regulation of Traditional Medicines in Australia

Chinese Herbs are now being used legally in Australia. As with pharmaceutical drugs, the issue of safety is difficult to guarantee without controlled trials to demonstrate such purpose.

The volume of active constituent analysis (see Pharmacognosy & Toxicology References) is record in itself that if something were likely to be dangerous, it would have been demonstrated by now, at least in laboratory animals. Even so, the volumes used on animals are so great that a human would never ingest such an amount in a controlled trial. Clinical trials involve complete formulas, so any speculation about the effect of a whole formula delineated from its constituent parts does not allow for interactions of those parts (Xu *et al.*)

Listing makes no claims to efficacy but means that the product has been assessed against standards defined in Schedule 4 of the Therapeutic Goods Regulations. It would seem feasible to accept that as the TGA had already weighed the evidence available that would preclude a formula from its lists, the remaining formulas have been considered safe for public use. The fact that over 30 formulas were removed from the herbalists pharmacopea in Australia in 1989 when the Register was set up,

² This scale is considered outdated by menopause researchers, due to the majority of symptoms on the scale not being estrogen dependent

attests to this procedure. Many formulas applicable to peri and post menopausal women remain on the Register's list.

Rationale for Clinical trials

In Australia, it is important to separate out anecdote from clinical effect, as more women seek to use legally listed formulas as well as self-medicate vitamins and supplements. It is time to assess critically whether these strategies are clinically effective according to sound methodological application.

Costing.

In 1995 the cost of Chinese herbal medicines varied, but averaged around \$30 per month, plus practitioner consultation fees. The in-progress menopause study referred to in this document (Beer 1997) estimated that herbs would be required for 8 weeks to effect change in perimenopausal symptomatology.

Trial Progress

Over 1000 women had enquired about this study. While making initial phone contact, many had indicated dissatisfaction with HRT - wishing to avoid or come off HRT (side effects, no effects, actual cancer, contra indication), others did not wish to cycle, or they had increased risk factors for cancer in their family. Very few women contacted this author because they regularly avoided western medicine. This data had not been released for publication at the time of the review, but was presented to the World Menopause Congress in 1986, held in Sydney, Australia (Beer, 1997).

Summary

This report acknowledges that hormone replacement therapy is the most effective treatment option for women with perimenopausal vasomotor disturbance. It has examined the evidence that HRT has a persuasive role in prophylaxis for normal problems of aging. The premise is questioned that HRT is the most effective protection against CHD. The role of exercise and other health related behaviours was not examined in relation to cardiovascular health, nor bone health. Osteoporosis was not examined, as estrogen benefits are not questioned.

The problems of estrogenic benefits creating increased risks of cancers, appear modulated by the addition of progestogens. There is evidence or concern that the addition of progestogens, decreases the beneficial gains created by estrogens alone. Women are not prepared to continue with cyclical bleeding, or they are not prepared to put up with uncomfortable side- effects. For some women, estrogens are contra-indicated. Someone must start to listen to what women want, not treat them as a cohort that assumes they only need to be educated to see the benefits of HRT.

Phytoestrogens in the form of food supplements, or as herbal medicines were examined. Some benefit appears to be derivable from soy proteins. Most focus placed the role of Chinese herbal medicine in the context of the current Australian setting.

Conclusion

The benefits of estrogen are modulated by progestogens. HRT has a role to play in the management of perimenopausal symptomatology and post menopausal prophylaxis. The risks and benefits of HRT must be decided individually, as each woman has her own priorities, which may not be the same as the medical professions'. Self- help is largely based on unsupported ideas. While self - medicators pay for their treatments, or seek alternative therapy practitioners, the cost of these strategies to the government appears low. If these strategies can be demonstrated to be effective, then they should be encouraged. Meanwhile, the alternative studies examined offer encouraging pilot results to warrant further studies.

References

Akiracao, K.; Seili, T.; Ichiro, O.; Ineko, N.; Hsinko, A. and Akirocao, Y. (1979) "The experimental use of Tsumera-Made preparations in treating Climacteric disturbances and indefinite post-surgical complaints." *Medicinal Therapy* **12** (9) translated in *Bull* OHAI (1984).**9** (7) 366-7

Antunes, C.M.F.; Stolley, P.D.; Roeenshein, N.B.; Davies, J.L.; Tonascia, J.A.; Brown, C.; Burnett, L; Rutledge, A.; Pokempner, B.A. and Garcia, R (1979) "Endometrial cancer and estrogen use" *New England Journal of Medicine* **300** (1) :9-13

Ballinger, C.B. (1985) "The menopause and the climacteric." in Priest, R.G. (Ed.) *Psychological Disorders in Obstetrics and Gyneaecology*. Butterworths. London

Barret- Connor, E. and Bush, T.L.(1991) "Estrogen and coronary heart disease in women" *J. Am. Med Assoc.* **265** : 1861-7

Beer, S.L. (1990) "Menopausal attitude survey" Independent Research Project. Course work requirement for Grad. Dip Women's Health. University of Melbourne. Unpublished material.

Beer, S.L. (1997) Chinese Herbal Medicine- A treatment for perimenopausal hot flushes? *Maturitas* **27** (Supplement 1): 214

Beer, S.L. (1997) The Alternative Treatment Seeker- Who Wishes to Avoid Hormone Replacement Therapy & Why? *Maturitas* **27** (Supplement 1): 215

Blatt, M.H.G. ; Weisbader, H. and Kupperman, H.S. (1953) "Vitamin E and climacteric syndrome.

Failure of effective control as measured by Menopausal Index." AMA Archs Intern Med. 91: 792-799

Chenoy, R;, Hussain, S.; Tayob, Y.; O'Brien P.M. S.; Moss, M.Y. & Morse, P.F. (1994) "Effect of oral gamolenic acid form evening primrose oil on menopausal flushing " *BMJ* **308** 501-503

Clayden, J.R.; Bell, J.W. and Pollard, P. (1974) "Menopausal flushing; Double blind trial of nonhormonal medication *Br. Med J.* **1** :341-344

Colditz, G.A.; Stampfer, M.J.; Willett, W.C.; Hennekens C.H.; Rosner, B & Speizer F.E. (1990) "Prospect study of estrogen replacement therapy and risk of breast cancer in post-menopausal women." *J.Am Med Assoc* **264** (20) :2648-2653

Cummings, S.R ; Black, D. and Rubin, S. M. (1989) "Lifetime risks of hip, Colle's or vertebral fracture, and coronary heart disease among white post-menopausal women." *Arch Int. Med.* **149** :2445-8

Cummings (1991) "Benefits and risks of long-term postmenopausal hormone therapy." in Samisioe, G (ed) 1991. *Cardiovascular disease and HRT. New Perspectives.* Park Ridge. Parthenon Pub. Group

Dennerstein, L. (1978) "The Menopause." in Dennerstein *et al. Gynaecology, Sex & Psyche.* Melbourne University Press. 179-192

Dharmananda, S (1988) "The deviation of Bupleurum & Peony formula and its use in the treatment of Pre-menstrual syndrome and menopausal distress," *Chinese Herbology*. Oriental Healing Arts Institute. Longbeach, CA, USA

Düker, E.M.; Kopanski, L, Jarry, H. and Wuttke, W. (1991) "Effects of extracts from *Cimicifuga racemosa* on gonadotropin release in menopausal women and ovariectomized rats" *Plant Med* **57** :420-424

Flaws, B (1992) "Jue Jing Qian Hou Zhu Zheng. Menopausal Syndrome" in *My Sister the Moon. The Diagnosis & Treatment of Menstrual Diseases by Traditional Chinese Medicine*. Boulder, Blue Poppy Press

Flaws, B (1993). How to Write a TCM Prescription. Boulder, Blue Poppy Press.

Goble, A.J. "Coronary heart disease in women in Australia. " in Kelly, D.T. (ed) 1992 *Women and Coronary Disease.* Edgecliff. Exerpta Medica

Goss, Newfeld , Libow *et al* (1988) "Autopsy study of the elderly institutionalised patient. Review of 234 autopsies. "*Arch Int Med* **148** 173-6 cited by Goble, in Kelly, D.T. (ed) 1992 *Women and Coronary Disease*. Edgecliff. Exerpta Medica.

Haines, C.J.; Chung, T.K.H.; & Leung, D.H.Y. (1994) "A prospective study of the frequency of acute menopausal symptoms in Hong Kong Chinese women "*Maturitas* **18** : 175-181

Hunter, M.S. "Emotional well-being, sexual behaviour and hormone replacement therpay" *Maturitas* (1990) **12** :299-314

Igarashi, M. (1988) "Efficacy of Kampo medicines in obstetrical and gynecological diseases." in *Hosoya, E. & Yamamura, Y. (Eds) Recent Advances in the Pharmacology of KAMPO (JAPANESE HERBAL) MEDICINES.* Excerpta Medicia, Sydney.

Ishino, S,(1992) 'Climacteric Disorders' in special supplement 'The ABC of Kampo Treatment' *The Journal of the Japanese Medical Association*, **108** (5) 150-152

Kaldas, R.S. & Hughes, C.L. (1989) " reproductive and general metabolic effects of phytoestrogens in mammals" *Reprod Toxicol* **3** : 81-89

Kano, T & Nishikawa, K. (1985)a 'Kampo-drugs Therapy for conjugated Estrogen-resistant Menopausal Syndrome of Autonomic Imbalance Type' *Jap. J.Fert. Ster.*, **30** (2) 205-214

Kano, T & Nishikawa, K., (1985)b 'Kampo-drugs Therapy for Insufficiency of Ovarian Function Accompained with Menopausal Complaints' *Jap.J. Fert. Ster.*, **30** (3) 367-376

Kaufert, P.A.; Gilbert, P. and Hassard, T. (1988) "Researching the symptoms of menopause: an exercise in methodology." *Maturitas*, **10**: 117-131

Koyama, T.; Hagino, N.; Cothron, A. and Saito, M. (1988) "Effect of combined treatment with Tokishaku-yaku-san (TJ-23) and human menopausal gonadotrophin on follicular maturation and ovulation in immature female rats." in Hosoya, E. and Yamamura, Y. (Eds) *Recent Advances in the Pharmacology of KAMPO(JAPANESE HERBAL) MEDICINES*. Excerpta Medicia. Sydney.

Kronenberg, F. (1990) "Hot flashes: Epidemiology and Physiology." in Flint, M. & Utian, W. (eds.) *Multidisciplinary Perspectives on Menopause, Ann. N.Y. Acad. Sci.* New York Academy of Sciences.

Kuno, Y. (1985) Human Perspiration. Charles C Thomas Springfield USA

Lightman, S.L.; Jacobs, H.S.; Maguire, A.K.; McGarrick, G. and Jeffcoate, S.L. (1981) "Climacteric flushing: Clinical and endocrine response to infusion of naloxone." *Br.J. Obstst. Gynecol.* **88** :919-924

Linsell, C.R. and Lightman, S.L. (1983) "Postmenopausal flashes : studies of chronological organisation." *Psychoneuroendocrinology.* **8** (4) : 435-440

Llewellyn-Jones, D. (1986) Every Woman 4th Ed. Faber & Faber. London

Lock, M.; Kaufert, P. and Gilbert, P. (1988) "Cultural construction of the menopausal syndrome. Japanese case." *Maturitas* **10** 317-332

Lock, M (1986) "Ambiguities of aging: Japanese experience and perceptions of menopause" *Cult. Med Soc* **10** : 23-46

Meldrum, D.,;Shamonki, I.M.; Frumar, A.M.,;Taltaryn, I.V.,; Chang, R.J. & Judd, H.L., (1979) 'Elevations in skin temperature of the finger as an objective index of postmenopausal hot flushes: Standardization of the technique' *Am. J. Obstet. Gynecol.*, 135 :713

Mitani, W. (1985) "Kampo treatment of Climacteric Disorder" J Trad Sino-Japanese Med 6 (3):47-51

Mochimaru, F.; Toyama, M.; Kanakuno, Y. & Inde, S. (1984) 'Objective indicator for the assessment of postmenopausal hot flushes' *Acta Obst Gynaec Jpn*, **36** (4) 643-645.

Morse, C. (1989) Menopausal Mood Disorders. Comprehensive Therapy. 15 (3):22-27

Murkies, A.L. ; Lombard, C. Strauss, B.J.G.; Wilcox, G. Burger, H.G. and Morton M.S. (1995) " Dietary flour supplementation decreases post-menopasual hot flushes : effect of soy and wheat. " *Maturitas* **21** 181-195)

Rose, D. P. (1992) "Dietary fibre, phytoestrogens, and breast cancer' Nutrition 8:47-51

Shibata, M. (1970) 'Pharmacological studies on *Bupleurum falcatum* L. Correlation between experimental pharmacological results and clinical applications of *Bupleurum*' Yakugaku Zasshi, **90** (3) 398-404

Smith, R.N.J.; Holland, E.F.N.; & Studd, J.W.W. (1994) "The symptomatology of progestogen intolerance" *Maturitas* **18** 87-91

Sturdee, D.W.; Wilson, K.A.; Pipili, E. and Crocker, A. (1978) "Physiological aspects of menopausal hot flush. *BMJ* 8 July : 79-80

Stampfer, M.J. (1991) "Oestrogen replacement therapy and coronary heart disease : a quantitative assessment of the epidemiological evidence." *Prev. Med.* **1** : 47 -63

Swan, N (1994) "The Health Report", Radio National, August

Takagi, K. & Shibata, M. (1969) 'Pharmacological studies on *Bupleurum falcatum* L. I. Acute toxicity and central depressant action of crude saikosides' *Yakugaku Zasshi* **89** (5) 712-720

Taltaryn, I.V.; Lomax, P.; Meldrum, D.R.; Bajoreck, J.G.; Chesarek, W. & Judd, H.L. (1981) "Objective techniques for the assessment of post-menopausal hot flushes." *Obsts. Gynecol.* **57** : 340 -344.

Tang, G. (1991) "Menopause: A study of women factory workers in Hong Kong." Personal communication author's transcript

Thomas, D.B. (1984) "Do hormones cause breast cancer? Cancer 53:594-604

Utian, W. (1972) "The true clinical features of postmenopause and oophorectomy, and their response to oestrogen therapy. *S. Afr. Med. J.* 46 :737-737

Voda, A. & Eliasson, M. (1983) Menopause: The Closure of Menstrual Life in Golub, S. (Ed) *Lifting The Curse of Menstruation.* Women and Health, Volume 8 Numbers 2/3

von Eickstedt, K-W. and Lang, M. (1989) "Sex hormones and related compounds including hormonal contraceptives." in Dukes, M.N.G. and Beeley, L. (Eds.) *Side Effects of Drugs Annual 13. A worldwide yearly survey of new data and trends.* Elsevier. Amsterdam, New Yrok, Oxford.

Wolf, H.L. (1993) *Menopause A Second Spring- Making A Smooth Transition with Traditional Chinese Medicine*. Boulder : Blue Poppy

Wren, B.G. & Brown, L.B. (1986) "Double-blind trial with clonidine and a placebo to treat hot flushes." Med J. Aust. **144** :369-370

Xiao, P-G., & Chen, K-J., (1987) 'Recent advances in clinical medicinal herbs' *Phytotherapy Res.* **1** (2) :53-57

Xu, R-S.; Zhu, Q-Z.,& Xie, Y-Y. (1985) 'Recent advances in studies on chinese medicinal herbs with physiological activity' *Journal of Ethnopharmacology*, 14 :223-253

Pharmacognosy & Toxicology References

Bensky, D. and Gamble, A. (1986) *Chinese Herbal Medicine Vol 1. Materia Medica* Eastland Press Inc. Seattle. USA.

Bi Chun-sheng (1986) "Bai Zhu" in Chang & But (1986) : 374-379

Chang, H.M. & But, P. P-H. Eds. (1986) *Pharmacology and Applications of Chinese Materia Medica, Vol* 1 World Scientific Publishing Co. P/L Singapore

Chang, H.M. & But, P.P-H. Eds. (1987) *Pharmacology and Applications of Chinese Materia Medica, Vol* 2 World Scientific Publishing, Teaneck, NJ .USA

Chow, H-Y et al (1976) Am J.CM 4 (1): 47 cited by Zhang Z-Y "ZhiZi" in Chang & But (1987): 1007

Chu, Y.(1986) "Gan Cao" in Chang & But (Eds): 304-317

Cyong, J. & Otsuka, Y. (1982) "A pharmacological study of the anti-inflammmatory activity of chinese herbs. A review." *Acupuncture & Electro-Therapeutics Res., Int. J.* **7**: 173-202

Gong, X-L (1987) "Bo He" in Chang & But (1987) : 1246-1249

Harada, M. ; Yamashita, A. and Aburasa, M. (1972) "Pharmacological studies on thr root bark of Paeonia Moutan 11 " *Yakugaku Zasshi* **92** : 750-756

Harada *et al.* (1969) *Journal of the Pharmaceutical Society of Japan (Tokyo)* **89** (9) :1205 cited by Huang, L-Y "Mu Dan Pi " in Chang & But Eds 1986: 618

Hosono *et al,* (1970) *The Journal of Society for Oriental Medicine in Japan* **21** (1) : 8 cited by Wang Y-S "Chai Hu " in Chang & But (eds) 1987: 967-974

Inooku, K. (1977) cited by Liao N-G "Dang Gui" in Chang & But (1986): 502

Lin, J-K and Wang, C.J. (1986) "Protection of crocin dyes on the acute hepatic damage unduced by aflatoxin B1 and dimethylnitrosamine in rats." *Carcinogenesis.* **7** (4) : 595-9

Nishoka, Otsuka, Kikudani. (1981) *Foundation and Applications of Kampo* Yaku Gi Xin Po Sha, Tokyo. (Fumi Horiguchi, trans; Peter Townsend back translation)

Qian, YL et al. (1979) Acta Academiae Medicinae Luzhou (3):1 cited in Yuan (1986)

Shibata, M. (1970) "Pharmacological studies on *Bupleurum falcatum* L . 111.Correlation between experimental pharmacological results and clinical applications of *Bupleurum*." Yakkugaku Zasshi **90** (3):398-404

Takagi, K. and Shibata, M. (1969) "Pharmacological studies on *Bupleurum falcatum* L. 1. Acute toxicity and central depressant action of crude saikosides." *Yakugaku Zasshi* **89** (5) : 712-720

Takechi, M. & Tanaka, Y. (1982) "Anti-viral substances from the root of Paeonia species" *Planta Med* **45** : 252-253

Wang, Y. & Ma, R. (1990) "Effect of Paeonia lactiflora on the blood coagulative and fibrinlolytic enzymes" *Chung Hsi Chieh He Tsa Chih* **10** (2) : 101-2

Yamauchi, K.; Fujimoto, N.; Kuwano, S.; Inouye, H. and Inoue, K. (1976) "Mechanism of purgative action of geniposide, an iridoid glucoside of the fruit of gardenia, in mice." *Planta Med* **30** : 39-47

Yuan W. (1986) "Sheng Jiang " in Chang & But (1986) :366-369