F 01 (Ratanakosin)

A Comparison of the Effects of Oral and Percutaneous Oestradiol on the Lipid Profile and on Atheroma Formation

C.J. Haines*, N. Panesar*, A.E. James*, T.J. Ngai*, D.S. Sahota*, R.L. Jones*

Oestrogen replacement therapy may be prescribed orally or else in a variety of formulations where the delivery avoids the hepatic first pass effect. The aim of this study was to compare the effects of oral and percutaneous oestradiol on the lipid profile and on atheroma formation. A hypercholesterolaemic female rabbit model was used. The study was of 12 weeks duration. Ovariectomized rabbits were divided into 3 groups, all receiving a 1.0% cholesterol diet. Group 1 rabbits acted as controls. Group 2 rabbits received 0.3 mg/kg percutaneous oestradiol (Oestrogel) daily whilst Group 3 rabbits received 0.1 mg/kg of oral oestradiol (Estrofem) daily. Blood was taken before the commencement of treatment for the measurement of concentrations of total cholesterol (TC), HDL-cholesterol and triglycerides (TG). The rabbits were sacrificed at 12 weeks and lipid measurements were repeated. Computerized image analysis was used to determine the amount of atheroma/cm^2 in the aorta. The changes in concentrations of the lipids and lipoproteins are shown below.

Gp	TC		HDL-C		TG	
	0	12	0	12	0	12
1	0.99 (0.21)	36.4 (8.67)	0.63 (0.16)	0.41 (0.09)	1.23 (0.81)	1.60 (0.94)
2	1.23 (0.76)	32.2 (9.05)	0.61 (0.17)	0.57 (0.10)	0.99 (0.39)	1.59 (1.75)
3	1.41 (0.63)	38.4 (8.10)	0.60 (0.12)	0.45 (0.13)	0.84 (0.37)	1.80 (1.03)

After 12 weeks there were significant increases in the concentrations of TC in all groups. There was no significant difference in TC concentrations between the 3 groups. There was a highly significant reduction in atheroma formation in Groups 2 and 3 compared with Group 1. These results suggest both oral and percutaneous oestradiol have a direct protective effect on the cardiovascular system independent of serum concentrations of total cholesterol.

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Free Communication - Thursday

F 02 (Ratanakosin)

Factors of Importance for Bone Mass in Swedish Middle Aged Women

L. Holmdahl*, G. Samsioe*, J. Lidfeldt*, C.D. Agardh*, L. Lindholm*, C. Nerbrand*, B. Scherstén*

In Sweden, 50% of the female population will sustain a fragility fracture during their lifetime. Preventive measures to individuals at high risk are likely to give an acceptable cost-benefit ratio. Identification of positive and negative risk factors for osteoporosis warrants high priority.

All women 51 to 60 years, living in the Lund area (N = 10,112), were offered a health assessment program including blood glucose, lipid profile and blood pressure. BMD of the wrist was performed, using DEXA. All women replied to a questionnaire, comprising information on physical activity, dietary, alcohol and smoking habits, family history of osteoporosis, present disease, hormonal status, weight gain/loss and ADL function. They were divided into three subgroups, according to hormonal status; premenopausal (PM), postmenopausal with (PMT) or without HRT (PMO).

Results are based on data from the first 1800 women. 17% were PM, 35% PMT, and 48% PMO. In the highest BMD quartile, (T-score -0,3 to 2,8), 15% were PM, 38% PMT and 47% PMO. Bone mass showed a positive correlation to BW in all subgroups. In PM we found a positive correlation to HDLC. In the lowest quartile (T-score -4,8 to -1,6), 8% were PM, 27% PMT and 65% PMO. We confirmed positive correlations to BW (all subgroups), and negative - use of alcohol (PM and PMO), smoking (PM and PMO) and family history (PMO and PMT), but found also positive correlations to blood pressure (PMO), triglycerides (PMO), total cholesterol (PMT) and HDLC (PMT).

Factors of importance for bone mass should be identified to minimize the impact of osteoporosis. Relations between blood lipids, blood pressure and bone density suggest that the metabolic syndrome could play a role in bone mineral metabolism.

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F 03 (Ratanakosin)

2D/3D Examination of Bone Structures in Patients and Bone Samples Using High Resolution Peripheral Computed Tomography and Micro-Tomography

M.A. Dambacher*, M. Neff*, B. Koller*, P. Rüegsegger*

The geometry of bone structures is a cardinal factor in bone strength. With aging and during disease the integrity of bone microarchitecture may be changed such that "osteoporotic" fractures often occur without significant density changes. In patients (in praxi) we visualized the bone microarchitecture with a lateral resolution of 200 µm with a high precision pQCT system and quantified the mineralisation of trabecular and cortical bone separately. Furthermore we analyzed for 3D stereologic parameters of unprocessed bone samples non-destructively down to a spatial resolution of 20x20x20 µm with a microtomography.

For the *in vivo* examinations we use a precise, accurate, low-dose, commercially available pQCT system (Densiscan 1000, Scanco Medical, Switzerland), which not only differentiates quantitatively between cancellous-bone and whole-bone density, for example of the distal radius (including carpal bones), the distal tibia, as well as whole-bone density of the diaphysis, but which also shows the structures of the bone volumes investigated, with a lateral resolution down to 0.3 or 0.2 mm. For the three dimensional morphometric evaluation of trabecular bone samples we use a commercially available microtomographic system (µCT20, Scanco Medical, Switzerland).

Our results show, for example, that increases in density occurring under the influence of sodium fluoride and bisphosphonates are closely linked to mechanical bone stress (formation fo micro-calluses) and that endocrinopathies such as hyperthyroidism or hyperparathyroidism show characteristic structural changes in trabecular and cortical bone, as do osteogenesis imperfecta, plasmocytomas, immobilisation, algodystrophy, aseptic necrosis and fractures.

Conclusion: Thin-multi-slice high-precision pQCT of non-weight-bearing and weight-bearing bones allows not only a differentiation between patients with low and high bone turnover or quantification of changes in bone density during treatment after only a few months (dynamic densitometry), but also subtile diagnosis with its high resolution of bone architecture and of different types of bone structure. On the other hand microtomography of bone samples is a fast, precise and non-destructive tool to give 3D information of the structures. These data can be used to estimate the internal forces in response to loads.

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Free Communication - Thursday

F 04 (Ratanakosin)

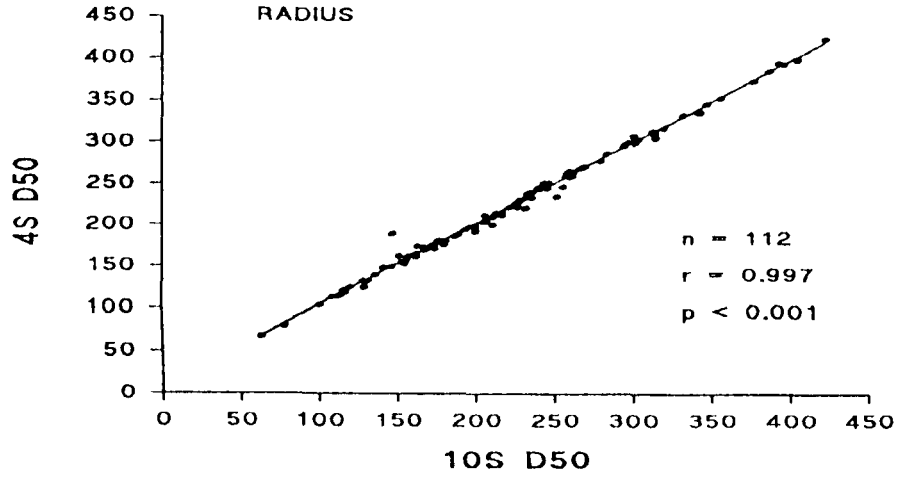
Assessment of the Risk of Osteoporosis Using High Resolution Peripheral Quantitative Computed Tomography (pQCT): A Comparison in Validity Between a Standard and a Reduced Bone Volume Measurement Procedure

M.A. Dambacher*, M. Neff*

Postmenopausal bone loss affects the trabecular bone first. Therefore methods for early risk-detection of osteoporosis in women should be specific for the trabecular bone.

The volumetric trabecular BMD (mg/cm^3) of 118 women between 31 and 80 years of age was measured in the distal radius of the non dominant forearm using high resolution pQCT (Densiscan 1000, Scanco Medical, Zurich/Switzerland). In contrast to the standard program with a stack of 10 measured tomograms slice thickness 1 mm, spacing 1.5 mm, evaluated bone volume 3-10 cm^3, first tomogram 7 mm proximal of the "endplate" of the radius the screening program measures only tomograms number 1, 4, 7 and 10 (total 4 slices), whereas the missing tomograms in between are extrapolated.

The results show that the 4 slice screening program is able to detect the true volumetric BMD of the trabecular bone in the distal radius. In contrast to this the measurement of skin thickness with ultrasound did not show such an excellent correlation.



Conclusion: The accuracy of the reduced 4 slice screening program specifically measuring trabecular bone volumetrically allow a reliable and early risk assessment in osteoporosis.

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F 05 (Ratanakosin)

Evaluation of Certain Clinical and Laboratory Changes in the Treatment of Post Menopausal Osteoporosis Between Hormonal Replacement + Calcium and Hormonal Replacement + Calcium + Vitamin D3 and Only Vitamin D3 + Calcium with Bearing Exercise

I.A. Rachman*, A. Hestiantoro*, A. Baziad*, F.A. Moeloek*, S. Sumosardjuno**

Post menopausal osteoporosis woman will be living with low level of estrogen also low level of vitamin D3 and cause more bone resorption than bone formation to extent that bone density deminish and osteopenia or even osteoporosis. Estrogen activated osteoblast in forming of collagen type I while vitamin D3 stimulates osteoblast for bone mineralisation. Both estrogen hormone and vitamin D3 have receptor at osteoblast which enchance the activity of osteoblast in bone formation. Due to the similar effect of both hormones to osteoblast, 59 cases of post menopause osteoporosis were studied (diagnosis with Lunar densitometer of WHO standard) and devided into 3 group of therapy: (1) Therapy A hormone replacement (HP) (Premarin 0,625 mg+Provera 5 mg)+calcium 400 gr; (2) Therapy B HP+calcium 400 gr+vitamin D3; (3) Therapy C calcium 400 gr+vitamin D3. All cases did a routine weight bearing exercise. The changes of bone density after 2 years treatment between A, B, C therapy are as follow:

	Lumbar % bone density up (+)				Femur % bone density up (+)			Radius % bone density up (+)
	L1	L2	L3	L4	Neck	Ward	Troch	
A therapy	+3,7%	+3,4%	+4,5%	+3,7%	+6,2%	+4,3%	+3,7%	+5%
B therapy	+7,4%	+4,6%	+9,1%	+5,9%	+9,5%	+9,2%	+9,4%	+6,8%
C therapy	+1,2%	+1,9%	+2%	+2,2%	+2,1%	+2,4%	+2,3%	+2,4%

The changes of osteocalcin and hidroksi piridinolin after 2 years treatment between A, B and C are as follow:

	Osteocalcin (N 3,7-1,0 ng/ml)			Hidroksi piridinolin (N 3,8-7,4 Nm)		
	Before	After	%	Before	After	%
A therapy	0,49-1,7	2,9-4,3	+29%	8,6-9,7	7,6-4,3	+3,3%
B therapy	0,38-2,4	3,2-5,2	+33,3%	6,9-9,4	8,2-5,2	-37,8%
C therapy	0,43-2,9	0,97-3,9	+6,8%	7,6-11,5	7,6-9,1	-16,8%

With B therapy (hormonal replacement+vitamin D3 calcium 400 gr) and weight bearing exercise give good result changes bone density in Lumbar, Femur and Radius than A or C from laboratory finding also seen that B therapy give a "bone formation" more than A or C therapy.

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Free Communication - Thursday

F 06 (Thonburi)

Study of Bleeding Pattern in Perimenopausal Woman with Levornorgestrel Intrauterine System (LNG-IUS) Providing Progestogenic Component of Hormone Replacement Therapy

S. P. Singh*

LNG-IUS (MIRENA) has been available in the U.K. since May 1995. It consists of a plastic T shaped frame with steroid reservoir around it's vertical stem which contains 52 mg Levornorgestrel releasing 20 mcg Levornorgestrel per 24 hours in the uterine cavity.

Objective: To study the bleeding pattern following insertion of LNG-IUS (MIRENA) in Perimenopausal women on Hormone Replacement Therapy (HRT) requiring contraception and suffering from menorrhagia, dysmenorrhea with or without organic pathologies fibroids, endometriosis etc and other bleeding irregularities after excluding malignancy.

Methods: Study was performed in general practice set up. Women aged 17-55 years (medium 36 years) attending the clinic were randomly selected. I have fitted 225 women with LNG-IUS over a period of 29 months since launched in the U.K. (30.5.95) under adequate analgesia after proper counseling and consent. 50 Perimenopausal women (22%) were fitted with LNG-IUS providing progestrogenic component of HRT with Oestrogen being given either orally or transdermally. 60% of them were suffering from self-reported clinically confirmed Menorrhagia, fibroids (12%), Endometriosis (3%). Serious pathologies were excluded by endometrial sampling and pelvic ultrasound (USS). Patients were followed-up 2, 6, 12, 18, 24 months and then yearly. Data were recorded on bleeding patterns, symptomatic improvement and side effects.

Results: 1-Highly effective contraceptive- no pregnancy recorded in 12-24 months. 2 - 6 to 24 months after insertion 50% became amenorrhoeic, 30% oligmenorrhoeic, with mean subjective reduction of menstrual blood loss (MBL) 85% (range 75% - 95%). 11% had occasional spotting requiring no protection. 5% had prolonged spotting 5 - 7 days monthly requiring panty liners with reduction of MBL (90-95%). Only 2% had regular but lighter periods with reduction of MBL (50-75%). 2% patients expelled the devices. No patients had heavy periods. 3-Surgical interventions were avoided in a majority of patients (98%) with an increase in hemoglobin concentration. 4:-Improvement of premenstrual symptoms (PMS) in significant number of patients.

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Conclusion:-LNG-IUS is an effective and novel way of providing progestogenic component of HRT with minimal systemic side effects, improving perimenopausal symptoms giving effective contraceptive protection along with additional gynecological benefits of reducing menstrual blood loss. (75%-100%), improving PMS, dysmenorrhoea along with significantly reducing cost by avoiding surgical interventions in a number of gynaecological conditions with high patient satisfaction and improved compliance of HRT.

Free Communication - Thursday

F 07 (Thonburi)

The Chemical Ablation of the Endometrium with Quinacrine in Cases of Functional Bleedings

I.V. Surcel*, A. Rosca*, C. Toader*, M. Petrescu*

Aims: This study presents a non invasive, efficient and cheap method for the treatment of functional bleedings, including those from perimenopause, using Quinacrine pellets.

Material and method: On 63 cases we used the chemical ablation of the endometrium with Quinacrine-Q. The sclerosing effect of Q on the endometrium is reducing his functional layer and, secondary the bleeding. The cases had bleedings of different causes-peri-menopause-59%, functional bleedings-27%, and other associated diseases-14%. The Q pellets and the intrauterine insertion are the same, as for chemical sterilization.

Results: Using 1 (22%), 2 (61%), 3 (11%) and 4 (5,4%) Q applications (252 mg each) the bleeding stops below 3 days, (76%), below 7 days (13%) and over 7 days in 13% of cases.

The therapeutic effect, the ceasing of the hemorrhage is obtained in 89% of cases.

The side effects are minimals-pelvic pain-in 12% of cases, fever-in 11%, uterine bleeding over 7 days in 4% and headache.

As conclusion, this method is simple as procedure, efficient and easy to perform.

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Free Communication - Thursday

F 08 (Thonburi)

Hysteroscopy in Women with Abnormal Uterine Bleeding on HRT: A Comparison with Postmenopausal Bleeding

F. Nagele*, F. Wieser*, A. Magos*

Almost 70% of all gynecological consultations in peri- and postmenopausal women are related to abnormal uterine bleeding (AUB). There is, however, relatively little data on the use of hysteroscopy in women taking HRT who develop AUB. The aim of this observational study was to determine the role of outpatient hysteroscopy in patients with AUB on HRT and to contrast this with a control group of women presenting with postmenopausal bleeding.

310/2203 women who were referred to our outpatient hysteroscopy clinic were included in this study. The study group included 157 women complaining of AUB on HRT, and the control group consisted of 153 cases with pure PMB. Outpatient hysteroscopy was performed using a 5 mm standard hysteroscope, and the uterine cavity was distended with carbon dioxide in the majority of cases. Local anesthesia was not administered routinely, and endometrial biopsy was performed if indicated.

Hysteroscopy was successful in 152/157 patients with AUB on HRT (97%) and in 12/153 with PMB (92%), respectively, and intrauterine pathology was diagnosed in 47% and 40% of these cases. Functional endometrium was noted significantly more often with HRT, and endometrial atrophy with PMB. Overall, local anesthesia was used in 41% of the cases, and shown to be significantly associated with need for cervical dilatation. Endometrial biopsy was attempted in 79% of the patients, but was unsuccessful significantly more often with PMB (39% *vs* 16%). There were six cases of endometrial cancer, all in the PMB group.

In conclusion, while there is a high incidence of intrauterine abnormalities in women with menstrual disorders while taking HRT, pathology is considerably different from those with PMB. Since focal lesions are commonly found in such patients, diagnostic hysteroscopy can be recommended as a means to improve the low compliance rate currently seen with HRT.

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Free Communication - Thursday

F 09 (Thonburi)

Balloon-Thermoablation An Optimal Standardized Organ Preserving Method for the Treatment of Menorrhagia

Ch. Kainz*, O. Preyer*, L. Hefler*, G. Sliutz*, C. Tempfer*

Menorrhagia is a problem with significant prevalence worldwide. Especially in perimenopausal women abnormal uterine bleeding due to benign conditions is a common problem. Periclimacteric bleeding disorders are often resistant to hormone therapy resulting in surgical interventions. Uterine thermal balloon endometrial ablation is a minimal invasive organ preserving treatment option.

The aim of our study was to evaluate treatment outcome, complications and feasibility of this new technique.

The principle is the destruction of the endometrium by heat delivered through a balloon catheter. The Cavatherm system uses an intrauterin silicon balloon catheter filled with glycin solution. The computer controlled setting produces a constant temperature of 75°C over a time period of 15 minutes at a pressure of 200 mmHg. An oscillating pump induces vigorous circulation of the balloon liquid to guarantee uniform heat distribution.

Fourteen patients were treated. During a follow-up period of six months 12 women reported satisfying results (3 amenorrhea, 7 hypomenorrhea, 2 normal menstrual bleeding). One patient on anticoagulation therapy required hysterectomy because of persisting severe uterine bleeding three weeks after thermoablation. One patient received endometrial resection because of persisting menorrhaghia. No intra- or postoperative complications were observed.

The main advantages of this new minimal invasive, organ preserving technique are the easy performance and good standardization through computer control. The method is safe and reveals a high percentage of patient's satisfaction.

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F 10 (Thonburi)

Uterine-Balloon-Therapy a Simple Endometrial Ablation Technique

Bernd Kleine-Gunk*

Menorrhagia is a common problem in pre- and perimenopausal women. Uterine bleeding as a result of HRT is usually disliked by postmenopausal women and one of the main causes of bad compliance.

Uterine Balloon Therapy (UBT) offers a new simple technique to treat benign uterine bleeding.

A latex balloon is introduced into the uterine cavity and then filled with glucose solution until a pressure of 160 mmHg is reached. The fluid in the balloon is then heated to 87°C. Therapy time takes 8 minutes only. Thus thermal destruction of the endometrium is acchieved.

UBT is simple to use. It can be done in an office setting under local anaesthesia. An international multi-center-study showed a success rate of 90%.

The results are comparable to those acchieved by hysteroscopic endometrial ablation. With more than 2000 therapies performed so far, no major complications have occurred.

Up to now UBT has mainly been used to treat menorrhagia in premenopausal women. This presentation discusses its role in the treatment of uterine bleeding under HRT. Because of the high rate of complete amenorrhea acchieved by this simple technique UBT might help to improve compliance of HRT in patients that otherwise do not tolerate HRT-induced uterine bleeding.

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Free Communication - Thursday

F 11 (Ayuthya)

Vaginosonographic Surveillance of Menopausal Women During Hormone Replacement Therapy

P. Frigo*, Christine Lang*, M. Metka*, W. Eppel*, M. Sator*, J. Huber*

Study aim: It was the aim of our study to examine the effects of hormone replacement on the size of the uterus and the development or increase of myomatas.

Patients and methods: In a prospective study 50 perimenopausal women were enclosed (53,8 ± 5,0 yrs). Patients received a substitution therapy composed of a combination of 4 mg estradiol valerate and 200 mg prasteronenantate (= Gynodian® Depot cartridges) given as a muscular injection in 6-10 week intervals (mean 7 weeks ± 4 days). Prior to the onset of therapy with Gynodian® and after a period of 12 months (± 13 days) a vaginosonography was performed. Measurements taken were length, thickness, height of endometrium, size of ovaries and of myomas, and data obtained were correlated with baseline findings.

Results: Within one year, significant increases in uterus length from 73.4 mm to 88.2 mm, in uterus thickness from 33.9 mm to 43.5 mm and in endometrium height from 4.1 mm to 6.7 mm were observed (median values). There was an increase in both the number (from 2.2 to 3.5) and the size of the myomatas (29.4 mm to 35.0 mm diameter). A statistical analysis conducted by means of the Wilcoxon matched pairs signed-rank sum test showed $p < 0.001$.

Conclusion: Our study shows that hormone substitution may have an impact on uterus growth and that therefore vaginosonographical monitoring can be recommended.

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F 12 (Ayuthya)

The Role of Endovaginal Ultrasound in Hormone Replacement Therapy

Song-Nan Chow*, Chien-Chu Huang*, Yu-Hong Lin*

Introduction : At present, a cut-off level of 5 mm for endometrial thickness is widely accepted for a screening program for endometrial carcinoma. However, under hormonal treatment, endometrium will become thicker. Therefore, we design this study to define an appropriate guideline for the follow-up of endometrial change during HRT.

For this purpose, endovaginal ultrasound will play a more accurate and important role.

Materials and Methods: Menopausal status is defined as serum FSH > 50IU/I and E2 < 20 pg/ml. 85 patients fulfilled this criteria have enrolled in our study till now. Pre-treatment endometrial thickness is measured by endovaginal ultrasound. Conjugated equine estrogen (Premarin) 0.625 mg/d for 25 days and medroxyprogesterone acetate (Provera) 5 mg/d for 14 days per month are prescribed. Follow-up sonography is performed at 1 month, 3 months and 6 months later and on 22nd or 23rd day of the cycle before withdrawal bleeding occurs. Endometrial Pipelle biopsy is performed after 6-month treatment and pathologic diagnosis is made. But endometrial biopsy is performed initially if pre-treatment endometrial thickness is greater than 5 mm.

Result: We have got 36 pathologic diagnosis till now. 5 women with initial endometrial thickness greater than 5 mm are proven to be simple hyperplasia in 1, complex hyperplasia in 1, endometrial polyp in 2 and normal pathology in the last one. 3 women with initial endometrial thickness less than 5 mm but with abnormal pathology are suspected after 1 month treatment due to unusual thickening of endometrium and proven 3 months later. Endometrial polyp is found in 2 patients and atypical complex hyperplasia is noted in the other one. Endometrial thickness of the other 28 women with normal endometrial pathology is (2.6 ± 0.8) mm, (4.0 ± 1.3) mm, (4.6 ± 1.5) mm, and (3.8 ± 1.2) mm in pre-treatment, 1st month, 3rd month, and 6th month, respectively. The differences in endometrial thickness between pre-treatment and other courses are all statistically significant. But no differences are noted between 1st month, 3rd month or 6th month. Finally, we found a cut-off level of 5.5 mm for endometrial thickness of postmenopausal women on hormone replacement therapy is quite reasonable. Its sensitivity, specificity, PPV and NPV is 100%, 90%, 77% and 100%.

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Discussion: From our present results, we find that endometrium will grow thicker significantly under HRT. However, the endometrial thickness won't have significant differences between 1-month, 3-month, or 6-month treatment. That is, the endometrial thickness will be stable during the treatment courses. Under HRT, we suggest that pre-treatment endovaginal ultrasound is neccessary and another one should be performed 3-6 months later to catch the pre-existing endometrial abnormality that was not found due to thin endometrium before treatment. However, we need more cases and longer time to follow-up these patients to get a more reasonable guideline for HRT.

F 13 (Ayuthya)

Comparison of Osteometer DTX-200 and Lunar DPX-L in the Measurement of Forearm Bone Mineral Density

Rojana Sirisriro*, Urusa Theppisai, Jittima Manonai**, Apichat Chittacharoen****

Since Ramathibodi has successfully implemented the menopause clinic, the number of patients refered for bone mineral density (BMD) measurement in the Department of Radiology has increased dramatically. The only clinical service bone densitometer (Lunar, DPX-L, USA) was insufficient for the patients' schedule. Thus a smaller dual energy X-ray absorptiometer (DEXA) unit for forearm BMD (Osteometer DTX-200, Denmark) was installed in the out patient department and was used to pre-select women who need BMD assessment of total body, hip and spine. The aim of this study was to correlate data from these two different DEXA units and to assess the suitability of using a smaller DEXA unit for screening of low forearm BMD. The subject included total 100 normal women (8 premenopause, 22 perimenopause and 70 menopause) age 37-77 y (average 52 y). BMD of the forearm was measured by both units. BMD of the ulnar, distal radius and ultradistal radius were compared. The results from regression analysis of the ultradistal radius BMD from both systems showed high correlation with r value = 0.976. The correlation of Z score of ultradistal radius (compare to the young adult match) from both units was also high (r value = 0.871) even the reference populations were different. There were poor correlation of the ulnar and moderate correlation of distal radius BMD. This was because of the interunit variability among bone densitometers in their different calibration procedures, algorithms, variability in photon source energies and intensities, including the choice of scan parameters and especialy the analysis procedures. Although there was such great variability, the analysis of BMD at the ultradistal portion of the radius did not show much different results because the BMD at the very distal portion of the bone which mainly composed of trabecular bone was selected and there was less interference from cortical bone. This study has shown high correlation of forearm BMD (ultradistal radius) measured by DTX-200 and DPX-L. At this point, we concluded that DTX-200 is a smaller unit, more economical and is comparable to the larger unit Lunar DPX-L for forearm (ultradistal radius) BMD measurement. In this specific circumstance, this small DEXA system is suitable for screening purpose for abnormal forearm BMD.

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Free Communication - Thursday

F 14 (Ayuthya)

Hormonal Profile in Young Women with Benign Breast Disease

Stanislaw Radowicki*, Rafal Koczorowski*, Katarzyna Skórzewska*

Benign breast disease (BBD) concerns about 50% women in the age 35-50, but it also develops in younger individuals, but in smaller percentage. Focus of analysis was to evaluate hormonal profile in young women with sonografically proven BBD. The analysis concerned women in reproductive, normally menstruated, without any hormonal distresses in hypothalamic - pituitary axis. In each case palpation and ultrasonographic investigation of breasts were done. The patients cohort was divided into two parts: BBD group - both USG and palpation positive, and control group when both investigations revealed nothing. From control cohort the representative group was randomised chosen. Blood samples from all patients were taken and concentration of estradiol, progesterone, testosterone, FSH, LH and PRL estimated.

BBD was found in 51 cases. Mean age 29,84 ± 8,60 ys (from 15 - 45). Controls: 36 patients in age from 17 to 40 ys (mean 26,9 ± 6,06).

Hormonal profile $\bar{x} \pm SD$	Control group n = 36	BBD group n = 51
FSH (U/l)	5.8 ± 2.895	5.65 ± 6.576
LH (U/l)	6.5 ± 3.642	5.6 ± 7.601
PRL (μIU/ml)	214.65 ± 84.369	208.85 ± 198.528
Testosterone (mmol/ml)	2.262 ± 2.633	2.533 ± 3.022
Estradiol (mmol/ml)	0.1275 ± 0.0708	0.1681 ± 0.1900*
Progesterone (mmol/ml)	9.54 ± 6.835	12.45 ± 12.093*

* difference statistically significant ($p < 0.05$)

Conclusion:

1. There is significant difference statistically in plasma concentrations of estradiol and progesterone.
2. No alternations in testosterone, FSH, LH and PRL levels between BBD group and controls were found.

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F 15 (Ayuthya)

Length of Menstrual Cycle among Women with Androgenic Syndrome

Stanislaw Radowicki*, Rafal Koczorowski*, Katarzyna Skorzewska*

Androgenization in women concerns about 5-10% of population in the reproductive age. The most common symptoms are: acne, hirsutism, alopetia, gain of body weight. These women often seek medical help because of menstrual disturbances or problems with fertility. Chosen first 1000 patients in Clinic of Endocrinological Gynecology, seeking specialist's opinion because of any dismember in the hypothalamus - pituitary - ovary axis. The diagnosis of the androgenic syndrome was made due to presence of at least two mentioned below symptoms: acne, hirsutism, alopetia, overweight (Body Mass Index > 30). In the time of the visit also investigated length of cycle (days), length and quantity of menstrual bleeding (days). Classified menstrual cycles into following six groups: primary amenorrhoea-lack of first menstrual bleeding up to 18 year of live, secondary amenorrhoea-break in menstruation longer then 6 months, intermittent amenorrhoea-cycle length from 42 days to 6 months, oligomenorrhoea - cycle length from 33 to 42 days, eumenorrhoea - cycle length 28 days ± 4 days, polymenorrhoea - cycle length shorter then 24 days. Focus of analysis was to evaluate the incidence of disturbances in the menstrual cycles affecting women with androgenization.

Androgenic syndrome was found in 104 cases (10.4%). Mean age of patients with androgenic syndrome: 26,9 ± 7,20 ys. (from 15 to 46). Menstrual cycle disturbances were found in 71 cases (68.27%): primary amenorrhoea - (23.07%), secondary amenorrhoea - 4 (3.84%), intermittent amenorrhoea - 3 (2.88%), oligomenorrhoea - 40 (38.46%).

1. Androgenic syndrome affects 10.4% women in the reproductive age with distempers in the hypothalamus-pituitary-ovary axis
2. Menstrual disturbances occur in 68% of women with androgenization.
3. The most common are : oligomenorrhoea (39%) and primary amenorrhoea (23%)

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Free Communication - Thursday

F 16 (Chiang Mai room)

Different Prevention of Bone Loss at Different Sites : Transdermal E2 *Versus* Calcium Over 4 Years

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Introduction: The present prospective study intends to compare the effect of transdermally applied 17-beta-Estradiol to peroral Calcium intake on bone density and biochemical parameters of bone turnover for up to 4 years.

Patients and Methods: 88 healthy postmenopausal women aged from 41 to 55 years (mean: 50.4) have been attributed to one of two matched groups and followed up to 4 years. Group A received 1000 mg Calcium Sandoz ff p.o./day. Group B has been substituted by 100 ug E2/day (Estraderm TTS 100) from day 1 - 21, combined with 10 mg Medroxy-Pogesterone-Acetate per os/day from day 12 to 21 followed by a treatment-free interval from day 22 to 28. BMC was measured at 0 and then every 6 months at the lumbar spine (*), the femoral neck (*) and the forearm (#). * = DPA, Novo BMCV-Lab 22-A, # = SPA, Novo GT 3T. The statistical evaluation within groups was done by students *t*-Test for paired data.

Results: *At the lumbar spine*, cyclic transdermal substitution by 100 ug Estradiol/d combined with 10 mg MPA/d protects, in contrast to peroral Calcium, efficiently from loss of BMC. Within 2 years, BMC increases significantly in the E2 group. *At the forearm* BMC is maintained in the E2 group, whereas there is a significant loss of BMC in the Calcium group. *At the femoral neck*, the same prophylactic effect cannot be found; BMC decreases in both groups. The different effect of E2 in comparison to Calcium on bone turnover is also documented on the different results in the biochemical analyses, such as alkaline phosphatase and the two-hours fasting urine parameters.

Conclusion: The prophylactic effect of HRT from postmenopausal bone loss varies greatly from site to site, dependent on its structure. But, at all sites, E2 is clearly superior to Calcium administration. However, Calcium seems to provide some benefits, too, when compared to nothing as stated in the literature.

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F 17

Continuous Combined Hormone Replacement Therapy (Kliogest®) in Singaporean Postmenopausal Women. A Randomised, Double-blind, Placebo-controlled Study

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The balance of risks and benefits of hormone replacement therapy (HRT) has been well documented in Caucasian women, but not among Asian women. A randomised, double-blind, placebo controlled study of the effect of oral 2 mg 17-beta-oestradiol + 1 mg norethisterone (Kliogest, Novo Nordisk A/S) on bleeding patterns, menopausal symptoms, plasma lipids, bone density and tolerability was carried out.

Forty-two Singaporean Chinese women (aged 46-64), diagnosed of menopause by surgical menopause or natural menopause were recruited to the study. The duration of treatment was 2 years and monitored at 3-6 months intervals. A decrease in irregular bleeding or spotting episodes over 24 months of Kliogest treatment was observed. Although the incidences of menopause symptoms were decreased in the patients receiving Kliogest treatment, there was no significant difference between the treatment and placebo groups. The total and LDL-cholesterol levels were significantly decreased while the HDL cholesterol level was significantly increased, with a consequent improvement in the HDL/LDL ratio. The bone mineral density level was increases in the Kliogest treatment group, however there was no significant difference between the treatment and placebo groups. The total alkaline phosphatase (bone formation marker) level was decreased significantly, indicating of a decrease in bone turnover. No weight gain or any adverse event related to treatment was observed.

In conclusion continuous Kliogest treatment appears to be well tolerated among the patients, improves the lipid profile and prevents bone loss. The results should instill some caution in interpretation due to the small number of patients studied.

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Free Communication - Thursday

F 18 (Chiang Mai room)

Is Cardio-vascular Protection Individually Predictable During HRT?

Bruno de Lignieres *

According to the largest animal and human data available today, the optimal prevention of cardio-vascular diseases observed in females is provided by ovarian secretion of 17ß-estradiol. Castrated females, post-menopausal women and men have an higher vascular morbidity and mortality independently of the classical risk factors. Ovarian secretion of 17ß-estradiol seems beneficial in all individuals, including subjects with obesity, high cholesterol levels, blood pressure and level of stress, or tobacco consumption. Optimum serum levels of estradiol providing a full impact on identified estrogen-dependent mechanisms seems to be achieved during mid-follicular-phase when reaching 60-100 pg/ml.

Several estrogens in different formulations with large inter-individual pharmacokinetic variation have been proposed to replace estradiol secretion, after menopause.

Because recent surveys do not show consistently positive results, specifically for thromboembolism and strokes, the hypothesis of different safety/efficacy ratio during different HRT must be investigated.

Simple mariners, if any, for checking the adequacy of each type of HRT to each single individual are highly desirable but do not seem to exist in the today current practice. No change in weight and blood pressure does not means that the vascular effects are optimal.

Lipoprotein changes are hardly interpreted when pregnancy-like effects, related to liver first-pass effect, are observed such as unsual parallel increase in HDL-C and triglycerides or paralled decrease in LDL-C and LDL-C particle size and when experimental models do not support their predictive value. Coagulation and fibrinolysis test are still no able to routinely detect changes toward thromboembolic risks for one individual, even if an increase in factor VII, fibrinopeptide A, prothrombin fragment 1+2 or decrease in antithrombin and protein S activities cannot be favourable. Several vasomotion test are proposed but not yet validated. Measurements of arterial wall thickness are also still experimental. Therefore without practical and cheap monitoring the use of oral estrogens, associated with pregnancy like side-effects on lipids an coagulation, may not be the first choice in women at risk such as obesity, tabacco consumption, history of thrombo-embolic accidents, heart disease, high

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blood pressure, dyslipidemia and diabetes. In such cases the risk of thromboembolism, including strokes, may be increased, instead of decreased.

Despite the urgent need to investigate non oral administration of estradiol closer to ovarian physiology (without first pass-effect and pregnancy-like side-effects), no one of the ongoing large prospective studies will deliver any information on this topic in the near future.

Free Communication - Thursday

F 19 (Chiang Mai room)

Progestins in HRT : What Role in Breast Cancer? A French Experience

Bruno de Lignieres*

Whether or not the additional use of progestins in HRT can influence the risk of breast cancer is still debated in 1998.

Few epidemiologic studies have enough statistical power to compare the relative risk in users of unopposed estrogen (a larger majority) and users of estrogen plus progestin users (less than 20% of users in most studies). In many countries the indications of the different doses and schedules of progestins are unclear, and many patients stop their treatment as soon as a bleeding has been induced, i.e. after less than 10 days in a high percentage of users. In France, a progestin treatment has been added to any estrogen in more than 80% of estrogen users and the duration of progestin exposure is more than 10 days per month in almost all cases.

- 2 previously published french studies looking at the breast cancer cases in postmenopausal women have shown more favourable prognosis factors in estrogen + progestin users than in non users. These results exclude a harmful effect of progestin on normal or malignant epithelial breast cells, and are in agreement with recent *in vitro* and *vivo* studies.
- One retrospective study conducted in NECKER hospital (Paris) has identified the incidence of breast cancer in the 10 to 20 years following a first presciption of HRT between 1971 and 1987, and in a control group never using HRT. Based on 101 cases of breast cancer, a slight increase in breast cancer incidence has been observed in users of unopposed estrogens, but not in users of estrogens consistently combined to progestins 10 or more days per month.

Therefore there is no evidence from France, a country with the highest rate of progestin prescriptions, that progestins used 12 to 25 days per month increase breast cancer morbidity. Existing data suggest that such prescription are more likely to be protective and to decrease mortality.

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F 20 (Chiang Mai room)

Amenorrhea, Regular and Irregular Bleeding During HRT

Bruno de Lignieres*

Bleeding during HRT is more likely to induce anxiety, unpleasant and relatively expansive intra-uterine examinations and finally drop-out if it occurs out of the predicted schedule.

A large variation in the observed incidence of "irregular"? bleeding, from 0 to 40% of the cycles or from 0 to 59% of HRT users, appears in published studies. Several reasons may explain the discrepancies between the different studies.

The **definition** of "Irregular" or "Abnormal" bleeding is inconsistent for the users on cyclic regimens. In one study the main concern is the duration and intensity of bleeding and in one other the actual intra-individual variability in cycle length. When the onset of bleeding is considered as the main point, the reference period may include 50 to more than 70% of the treatments days. Then using the actual day of progestin withdrawal as a limit of onset for "regular" bleeding may double the apparent incidence of "irregular" bleeding in comparison with studies allowing an earlier 2 to 9 days before progestin withdrawal. However in this case the term of "withdrawal" bleeding is inappropriate and may be misleading. With the most favourable defintion (up to 9 days before withdrawal) a cyclic HRT using oral DEE induces "irregular" bleeding in less than 20% of cycles. With the more restrictive definition (the actual withdrawal) "irregular" bleeding is recorded in more than 40% of cycles.

The **duration** of the study seems to have a great influence on the results. The incidence of the "irregular" bleeding is shown to decrease with time in several studies being higher during the first 6 months of HRT than during the following months.

The first explanation may be related to the high rate of drop-out frequently observed during the first year of HRT and likely to select the users free of side-effects. Drop-out rate is quite high in large multi-centric studies but can be strikingly reduced in studies involving a small number of well motivated patients and physicians.

A second explanation is related to the possibility for patients to customize their HRT during the first months of HRT in selecting their own individual optimal dosages. Then

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this two explanations do not suggest that bleeding results actually improve with time during any given fixed HRT, but rather that the apparent improvement come from an individual adaptation of dosages if allowed, or from drop-out if not allowed.

A third explanation is the time elapsed since menopause. The longer this time, the lower the possibility to face some residual irregular ovarian activity able to induce irregular bleeding independently of HRT.

Obviously the major influence on bleeding pattern come from the **combination of progestin to estrogen**. The highest rate of cyclic bleeding (>80% of cycles) is obtained with a cyclic addition of progestin to estrogen leaving a unopposed estrogen phase of 7 or more days per cycle. On the contrary reducing or suppressing the unopposed phase strikingly reduce the rate of regular cyclic bleeding and increase the inicdence of amenorrheas to 60-94% of the cycles. However the highest incidence of irregular bleeding is observed with non-stop continuous combined regimen (27-38% of cycles) while interruption of the progestin treatment few days each month is associated with a lower incidence (5-16% of cycles). These results may be explained be the regulation of progesterone receptors in endometrial stroma.