



Women's Health Care Bibliography March 2004

1: Abdom Imaging. 2004 Mar 18 [Epub ahead of print]

Small bowel obstruction secondary to Crohn disease.

Zissin R, Hertz M, Paran H, Bernheim J, Shapiro-Feinberg M, Gayer G.

We investigated the computed tomographic (CT) findings in patients with small bowel obstruction (SBO) and Crohn disease (CD). Fourteen patients, seven men and seven women (mean age, 41.3 years), were retrospectively reviewed. All presented with clinical symptoms and signs of SBO. Eleven had a history of CD, whereas three experienced the bowel obstruction as the first manifestation of the disease. On CT, features of complete SBO were seen in nine patients, whereas incomplete obstruction was found in the other five. One patient had CT findings of an adhesive obstruction. The other 13 were diagnosed as having CD-related SBO; a markedly stenotic bowel segment caused the obstruction in one patient, and a thickened-wall small bowel segment with luminal narrowing was evident at the transition zone in the other 12. The mural thickening had a target appearance in seven and homogeneous thickening in the other five. Additional thickened bowel segments were found in five patients and mesenteric involvement was found in 10. Five patients were treated conservatively, and the other nine underwent surgery (one with adhesiolysis only). Resection of the stenotic bowel was performed in six patients and stricturoplasty was done in the other two, with associated intestinal biopsy in one of these two patients. Histopathology revealed findings of active on chronic disease in all. CT is frequently performed for suspected SBO, so radiologists should be aware of the diagnosis of CD, because SBO may be its first manifestation. Alternatively, radiologists can accurately diagnose a CD-related obstruction in a patient with known CD and differentiate it from an obstruction due to adhesions. Patient management in these cases, however, is based most often on the clinical condition.

PMID: 15024508 [PubMed - as supplied by publisher]

2: Am J Cardiol. 2004 Mar 15;93(6):805-8.

Risk for subsequent coronary artery disease after preeclampsia.

Haukkamaa L, Salminen M, Laivuori H, Leinonen H, Hiilesmaa V, Kaaja R.

We studied the history of hypertensive pregnancies and conventional risk factors in 141 relatively young (<66 years) parous women with angiographically documented coronary artery disease and in age-matched controls. Our study showed that hypertension, diabetes, hypercholesterolemia, advanced age, smoking, and preeclampsia are independent risk factors for subsequent coronary artery disease.

PMID: 15019902 [PubMed - in process]

3: Am J Cardiol. 2004 Mar 15;93(6):765-7.

Examination of gender bias in the evaluation and treatment of angina pectoris by cardiologists.

Blum M, Slade M, Boden D, Cabin H, Caulin-Glaser T.

One hundred fifty-eight patients (76 men and 82 women) presenting to an outpatient cardiology clinic with a new complaint of angina were prospectively followed to determine if there was a gender bias in the management of suspected coronary artery disease when physicians trained in cardiology managed their care. Overall, there were no differences in the percentage of women who underwent noninvasive evaluation, invasive evaluation, and treatment of suspected coronary artery disease compared with men.

PMID: 15019889 [PubMed - in process]

4: Am J Epidemiol. 2004 Mar 15;159(6):547-55.

Obesity and the risk of Parkinson's disease.

Chen H, Zhang SM, Schwarzschild MA, Hernan MA, Willett WC, Ascherio A.

Dopamine is involved in the regulation of food intake, and obese persons have decreased dopamine D2 receptor availability in the striatum. Furthermore, midlife triceps skinfold thickness has been found to be positively associated with the risk of Parkinson's disease (PD) among Japanese-American men in Hawaii. The authors prospectively investigated whether obesity was associated with PD risk in two large cohorts of US men and women. They documented 249 cases of PD in men (1986-2000) and 202 cases in women (1976-1998). Neither baseline body mass index (weight (kg)/height (m)²) nor early adult body mass index was associated with PD risk. The multivariate relative risk for a baseline body mass index of ≥ 30 versus < 23 was 0.8 (95% confidence interval (CI): 0.6, 1.2; p for trend = 0.3). Overall, waist circumference and waist-to-hip ratio were not related to PD risk. However, among never smokers, both variables showed significantly positive associations with PD risk. The relative risks for comparisons of extreme quintiles were 1.9 (95% CI: 1.0, 3.4; p for trend = 0.03) for waist circumference and 2.0 (95% CI: 1.1, 3.6; p for trend = 0.03) for waist-to-hip ratio. The results do not support a role of overall obesity in PD pathogenesis; however, central obesity may be associated with higher PD risk among never smokers, and this finding merits further investigation.

PMID: 15003958 [PubMed - in process]

5: Arch Gynecol Obstet. 2004 Mar 17 [Epub ahead of print]

The role of transvaginal colour Doppler sonography in evaluation of abnormal uterine bleeding.

Dragojevic S, Mitrovic A, Dikic S, Canovic F.

INTRODUCTION. Treatment of abnormal uterine bleeding understands a prompt diagnostic procedure, for the sake of defining the etiological factor of disease. The abnormal uterine bleeding is more common in the perimenopausal than in the postmenopausal women, and it is more frequent sign of an endometrial proliferative or hyperplastic changes. Fewer percentages of women with unexpected and/or acyclic and prolonged bleeding have endometrial cancer. **MATERIALS AND METHODS.** Seventy-one (71) patients with abnormal uterine bleeding, older than 40 years, of which 10 were in post-menopause, have been tested. Prior to explorative curettage and histopathological analysis, ultrasonographic and hemodynamic studies, at the uterine blood vessels level (uterine artery bilaterally) had been performed by transvaginal colour Doppler method. **RESULTS.** Histopathological results indicated

four types of represented changes, on the basis of how the patients were divided into the groups: I, proliferative endometrium-20 patients; II, endometrial adenocarcinoma-23 patients; III, various forms of endometrial hyperplasia-26 patients, IV, atrophic endometrium-2 patients. Significant statistical difference in the endometrial thickness was established between groups I and II, and endometrial cancer was not found in less than 8 mm thick endometrium. By analysing hemodynamic parameters, significantly lower PI values were obtained in the group of patients with pathologically altered endometrium, compared to other groups. **CONCLUSION.** Transvaginal colour Doppler has significant role in the diagnostic process for evaluation of abnormal uterine bleeding in perimenopausal and postmenopausal women. Doppler sonography can help in differentiating physiological from malignant endometrial changes and in deciding on the most efficient therapeutical regime.

PMID: 15029507 [PubMed - as supplied by publisher]

06: Arterioscler Thromb Vasc Biol. 2004 Mar;24(3):571-6. Epub 2003 Dec 29.

Effect of lower dosage of oral conjugated equine estrogen on inflammatory markers and endothelial function in healthy postmenopausal women.

Wakatsuki A, Ikenoue N, Shinohara K, Watanabe K, Fukaya T.

OBJECTIVE: Although oral estrogen replacement therapy (ERT) in postmenopausal women improves endothelial function, it also increases plasma C-reactive protein (CRP) and interleukin-6 (IL-6) concentration. The proinflammatory effect of oral ERT may explain the increased risk of coronary heart disease (CHD) associated with this treatment. Recent observational studies have demonstrated that a lower dose of oral estrogen reduces the risk for CHD. The purpose of the present study was to investigate the effects of low-dose oral estrogen on vascular inflammatory markers and endothelium-dependent vasodilation in postmenopausal women.

METHODS AND RESULTS: Postmenopausal women were randomized into 3 groups to receive no treatment (n=14) or oral conjugated equine estrogen (CEE) at a dosage of 0.625 mg (n=15) or 0.3125 mg (n=15) daily for 3 months. CEE at a dosage of 0.625 mg resulted in significant increases in plasma concentrations of CRP from 690.9+/-749.5 to 1541.9+/-1608.0 ng/mL, serum amyloid A from 6.12+/-4.15 to 8.25+/-4.40 microg/mL, and IL-6 from 1.45+/-0.73 to 2.35+/-1.16 pg/mL. In contrast, CEE at a dosage of 0.3125 mg had no effect on these inflammatory markers. Both dosages of estrogen significantly decreased E-selectin concentration, whereas the concentrations of intercellular and vascular cell adhesion molecules remained unchanged. In both CEE groups, flow-mediated vasodilation in the brachial artery was increased significantly, whereas nitroglycerine-induced vasodilation was unaltered. **CONCLUSIONS:** Oral CEE at a low dose of 0.3125 mg in postmenopausal women eliminated the adverse effects of high-dosage oral CEE on vascular inflammatory markers in addition to preserving the favorable effects of estrogen on cell adhesion molecules and endothelial function.

PMID: 14699021 [PubMed - in process]

7: Cancer. 2004 Mar 15;100(6):1145-51.

Restaging surgery for women with borderline ovarian tumors: results of a French multicenter study.

Fauvet R, Boccara J, Dufournet C, David-Montefiore E, Poncelet C, Darai E.

BACKGROUND: The purpose of the current study was to examine the surgical management of women with borderline ovarian tumors and the adequacy of initial staging according to the guidelines of the International Federation of Gynecology and Obstetrics; to evaluate the impact of restaging operations; and

to identify risk factors for initial understaging. METHODS: In a retrospective French multicenter study, 54 of 360 women with borderline ovarian tumors underwent a restaging operation. After excluding women with initial complete staging (n = 62), epidemiologic, surgical, and histologic parameters and risk of recurrence were compared between women who underwent restaging (n = 54) and those who did not (n = 244). RESULTS: One hundred fifty (41.6%) of 360 women underwent intraoperative histologic examination, which led to the diagnosis of a borderline tumor in 97 cases (64.7%). Thirty-seven (38.1%) of these 97 women had undergone complete initial staging procedures. A restaging operation was performed for 54 women. A lower median age and a higher rate of conservative treatment were noted in the group that underwent restaging. Eight (14.8%) of the 54 women who underwent restaging had their tumors upstaged: 7 of the 41 cases initially diagnosed as Stage IA tumors were upstaged to Stage IB (n = 3) or to Stage IIA, IIB, IIIA, or IIIC (n = 1 for each); in the eighth case, a Stage IC tumor was upstaged to Stage IIIA. Upstaging tended to be more common in women with serous borderline tumors (P = 0.06) and in women who underwent cystectomy (P = 0.08). There was no difference in recurrence rates according to whether a restaging operation was performed. The recurrence rates after conservative and radical treatment were 15.6% (25 of 160) and 4.5% (9 of 200), respectively (P < 0.001). CONCLUSIONS: Women who initially were diagnosed with Stage IA disease and who had serous borderline tumors or underwent cystectomy appeared to derive the most benefit from restaging surgery. Nonetheless, the indications for restaging surgery remain controversial, as no difference in recurrence rate was observed between women who underwent restaging and those who did not.

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PMID: 15022280 [PubMed - in process]

8: Cancer Causes Control. 2004 Mar;15(2):105-11.

A prospective study of induced abortion and breast cancer in African-American women.

Palmer JR, Wise LA, Adams-Campbell LL, Rosenberg L.

Objective : There continues to be controversy about whether induced abortion influences the risk of breast cancer. Because case-control studies of this relation are subject to recall bias, there is a need for prospective data. Further, there has been little study of abortion and breast cancer in African-American women. We assessed the relation of abortion to risk of breast cancer in a prospective follow-up study of African-American women. Methods : Black Women's Health Study participants have been followed by mailed questionnaires every two years since enrollment in 1995.

Participants reported

348 incident breast cancers during 205,983 person-years of follow-up. Women who had an induced abortion were compared with women who had never had one, with nulliparous and parous women analyzed separately. Incidence rate ratios (IRR) with two-sided 95% confidence intervals (CI) were derived from Cox regression models that controlled for age, age at first birth, number of births, history of spontaneous abortion, and other factors. Results : Among nulliparous women, the IRR for any induced abortion relative to none was 0.9 (95% CI = 0.5-1.4), and among parous women, the comparable IRR was 1.1 (95% CI = 0.8-1.4). Risk did not vary by number of abortions, age at first abortion, age at diagnosis or a family history of breast cancer in either nulliparous or parous women. Conclusions : Our findings indicate that induced abortion does not increase breast cancer risk in African-American women.

PMID: 15017122 [PubMed - in process]

9: Cancer Chemother Pharmacol. 2004 Mar 11 [Epub ahead of print]

The effects of degree of hepatic or renal impairment on the pharmacokinetics of exemestane in postmenopausal women.

Jannuzzo MG, Poggesi I, Spinelli R, Rocchetti M, Cicioni P, Buchan P.

PURPOSE. Two studies were conducted to compare the pharmacokinetics and tolerability of exemestane in postmenopausal subjects with various degrees of impairment of hepatic or renal function with those in healthy postmenopausal subjects. **METHODS.** All subjects were postmenopausal females. In study 1, nine subjects had normal hepatic function (Child-Pugh grade A), and nine had moderately (grade B) and eight severely (grade C) impaired hepatic function. In study 2, six subjects had normal renal function, and six moderately (creatinine clearance, CrCL, 30-60 ml/min per 1.73 m²) and seven severely (CrCL <29 ml/min per 1.73 m²) impaired renal function. Each subject took a single oral dose of 25 mg exemestane. Samples of plasma (to 168 h after dosing) and urine (to 72 h in study 1, or 96 h in study 2) were taken for pharmacokinetic analysis. Safety and tolerability were assessed by monitoring vital signs, laboratory safety tests, ECG and adverse events. **RESULTS.** Exposure to exemestane was increased two- to threefold in patients with hepatic impairment. Thus, the geometric mean AUC(0- infinity) values were 41.71 (90% CI 32.2 to 54.0), 99.02 (76.5 to 128.2) and 118.59 ng.h/ml (90.2 to 156.0) in healthy subjects, and in patients with moderate and severe hepatic impairment, respectively (P<0.01). C(max) also increased twofold. Compared with healthy subjects, patients with hepatic impairment had lower apparent oral clearance and apparent volume of distribution of exemestane. Renal impairment was also associated with two- to threefold increases in AUC(0- infinity): 34.64 (90% CI 23.9 to 50.2), 94.10 (64.9 to 136.4) and 65.52 ng.h/ml (46.5 to 92.4) in healthy subjects, and in patients with moderate and severe hepatic impairment, respectively (P<0.05). C(max) did not change significantly. Apparent oral clearance was directly correlated with CrCL (r²=0.43). Exemestane was tolerated well, with no safety concerns. **CONCLUSIONS.** Oral clearance of exemestane was reduced in the presence of significant hepatic or renal disease. However, in view of the relatively large safety margin and the mild nature of the side effects of exemestane, the therapeutic implications of these changes in pharmacokinetics are considered minor and of no clinical significance.

PMID: 15014897 [PubMed - as supplied by publisher]

10: Cardiovasc Diabetol. 2004 Mar 15;3(1):3.

Cardiovascular adaptations to exercise training in postmenopausal women with type 2 diabetes mellitus.

McGavock JM, Mandic S, Lewanczuk R, Koller M, Vondermuhl I, Quinney A, Taylor D, Welsh R, Haykowsky M.

Background: Type 2 diabetes mellitus (DM-2) is one of the most prevalent chronic diseases of the aged and contributes to a significant amount of cardiovascular disease morbidity and mortality. Exercise training may be beneficial in attenuating the cardiovascular maladaptations associated with DM-2. The purpose of this study was to examine the effects of exercise training on left ventricular (LV) and vascular function in a sample of postmenopausal women with DM-2. Methods: Twenty-eight postmenopausal women with DM-2 (age: 59 +/- 7 yrs) were assigned to either an exercise training (ET) (n=17) or control group (CT) (n=7). Cardiorespiratory fitness (VO₂peak), LV filling dynamics and arterial compliance were assessed at baseline in

all participants. The ET group performed a supervised aerobic and resistance training intervention three days per week for a period of 10 weeks, while the CT group continued normal activities of daily living. Results: Body mass index, VO₂peak, age and duration of diabetes were similar between the ET and CT groups at baseline. VO₂peak (21.3 +/- 3.3 to 24.5 +/- 4.2 ml/kg/min, p < 0.05) and large artery compliance (1.0 +/- 0.4 to 1.2 +/- 0.4 mL/mmHg, p < 0.05), increased significantly in the ET group following training despite no change in LV filling dynamics, blood pressure, lipid profile or insulin sensitivity. All variables remained unchanged in the CT group. Conclusions: Exercise training improves large artery compliance and cardiorespiratory fitness in post menopausal women with DM-2, without any appreciable changes in LV filling dynamics or conventional risk factors for cardiovascular disease.

PMID: 15023235 [PubMed - as supplied by publisher]

11: Circulation. 2004 Mar 16;109(10):e158-60.

Cardiology patient page. Heart disease prevention in women.

Mosca L.

PMID: 15023896 [PubMed - in process]

12: Circulation. 2004 Mar 15 [Epub ahead of print]

Blood Pressure and Risk of Secondary Cardiovascular Events in Women. The Women's Antioxidant Cardiovascular Study (WACS).

Mason PJ, Manson JE, Sesso HD, Albert CM, Chown MJ, Cook NR, Greenland P, Ridker PM, Glynn RJ.

BACKGROUND: In apparently healthy people, the relation between blood pressure and risk of subsequent cardiovascular disease (CVD) is linear. In persons with CVD, the relation is uncertain. **METHODS AND RESULTS:** We conducted a prospective study of 5218 older women with CVD who reported their blood pressure at baseline in the Women's Antioxidant Cardiovascular Study (WACS), an ongoing double-blind, placebo-controlled secondary prevention trial of the benefits and risks of antioxidant vitamins, folic acid, vitamin B6, and vitamin B12 among women with CVD or ≥ 3 coronary risk factors. A total of 661 confirmed CVD events (nonfatal myocardial infarction, nonfatal stroke, coronary artery bypass graft procedure, percutaneous coronary angioplasty, or CVD death) occurred during a median follow-up of 6.5 years. After controlling for age, randomized treatment assignment, antihypertensive medication use, and coronary risk factors, we found that systolic blood pressure (SBP) was a strong predictor of CVD events and that the relation between SBP and CVD risk was positive, continuous, and linear (P for linear trend=0.001). For each 10-mm Hg increment in SBP, there was a 9% (95% CI 4% to 15%) increase in risk of secondary CVD events. Diastolic blood pressure, mean arterial pressure, and pulse pressure were weaker predictors of CVD risk in this cohort, and joint consideration of SBP and diastolic blood pressure found that only SBP significantly predicted risk. Use of antihypertensive medication did not modify the relationship of SBP with CVD events. **CONCLUSIONS:** In this population of women with CVD, we observed a strong, continuous, and linear association between SBP and risk of secondary CVD events. SBP was the blood pressure measure most strongly related to CVD risk.

PMID: 15023883 [PubMed - as supplied by publisher]

13: CMAJ. 2004 Mar 16;170(6):983-94.

Clinical practice guidelines for the care and treatment of breast cancer: 15. Treatment for women with stage III or locally advanced breast cancer.

Shenkier T, Weir L, Levine M, Olivotto I, Whelan T, Reyno L; Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer.

OBJECTIVE: To define the optimal treatment for women with stage III or locally advanced breast cancer (LABC). **EVIDENCE:** Systematic review of English-language literature retrieved from MEDLINE (1984 to June 2002) and CANCERLIT (1983 to June 2002). A nonsystematic review of the literature was continued through December 2003. **RECOMMENDATIONS:** The management of LABC requires a combined modality treatment approach involving surgery, radiotherapy and systemic therapy. Systemic therapy: chemotherapy. Operable tumours. Patients with operable stage IIIA disease should be offered chemotherapy. They should receive adjuvant chemotherapy following surgery, or primary chemotherapy followed by locoregional management. Chemotherapy should contain an anthracycline. Acceptable regimens are 6 cycles of FAC, CAF, CEF or FEC. Taxanes are under intense investigation. Inoperable tumours. Patients with stage IIIB or IIIC disease, including those with inflammatory breast cancer and those with isolated ipsilateral internal mammary or supraclavicular lymph-node involvement, should be treated with primary anthracycline-based chemotherapy. Acceptable chemotherapy regimens are FAC, CAF, CEF or FEC. Taxanes are under intense investigation. Patients with stage IIIB or IIIC disease who respond to primary chemotherapy should be treated until the response plateaus or to a maximum of 6 cycles (minimum 4 cycles). Patients with stage IIIB disease should then undergo definitive surgery and irradiation. The locoregional management of patients with stage IIIC disease who respond to chemotherapy should be individualized. In patients with stage IIIB or IIIC disease who achieve maximum response with fewer than 6 cycles, further adjuvant chemotherapy can be given following surgery and irradiation. Patients whose tumours do not respond to primary chemotherapy can be treated with taxane chemotherapy or can proceed directly to irradiation followed by modified radical mastectomy, if feasible. Systemic therapy: hormonal therapy. Operable and inoperable tumours. Tamoxifen for 5 years should be recommended to pre- and postmenopausal women whose tumours are hormone responsive. Locoregional management. Operable tumours. Patients with stage IIIA disease should receive both modified radical mastectomy (MRM) and locoregional radiotherapy if feasible. They may be managed with MRM followed by chemotherapy and locoregional radiotherapy, or chemotherapy first followed by MRM and locoregional radiotherapy. Breast-conserving surgery is currently not a standard approach. Locoregional radiotherapy should be delivered to the chest wall and to the supraclavicular and axillary nodes. The role of internal mammary irradiation is unclear. Inoperable tumours. Patients with stage IIIB disease who respond to chemotherapy should receive surgery plus locoregional radiotherapy. The locoregional management of patients with stage IIIC disease who respond to chemotherapy is unclear and should be individualized. Patients whose disease remains inoperable following chemotherapy should receive locoregional radiotherapy with subsequent surgery, if feasible. **VALIDATION:** The authors' original text was revised by members of the Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer. Subsequently, feedback was provided by 9 oncologists from across Canada. The final document was approved by the steering committee. **SPONSOR:** The Steering Committee on Clinical Practice Guidelines for the Care and Treatment of Breast Cancer was convened by Health Canada. Completion date: December 2003.

PMID: 15023926 [PubMed - in process]

14: Contraception. 2004 Mar;69(3):251-7.

Oral contraceptive use and risk of diabetes among Chinese women.

Rosenthal AD, Shu XO, Jin F, Yang G, Elasy TA, Li Q, Xu HX, Gao YT, Zheng W.

Oral contraceptive (OC) use has been associated with alterations in carbohydrate metabolism. We examined the effect of OC use on the risk of diabetes among

Chinese women. A nested case-control study was conducted among 57,130 women screened for diabetes at enrollment for the Shanghai Women's Health Study, a population-based cohort study of Chinese women aged 40-70 years in Shanghai, China. Included in this study were 259 women newly diagnosed with diabetes and 2072 age-matched controls (8 controls per case), randomly selected from women who tested negative for urine glucose. Multivariate-adjusted odds ratios (OR) and 95% confidence intervals (CI) were used to measure the strength of the association between OC use and diabetes risk. Overall, OC use was not associated with the risk of diabetes. Stratified analysis by menopausal status revealed a dose-response relationship between the duration of OC use and the risk of diabetes among premenopausal women (p for trend = 0.02), with a 3.2-fold elevated risk observed among those who used OC longer than 1 year. Risk of diabetes diminished with increasing time since last OC use (p = 0.02). Use of intrauterine devices was associated with a reduced risk of diabetes in both pre- and postmenopausal women (OR = 0.67, CI: 0.48-0.93). These findings suggest that recent use (within 5 years) and continued use (>1 year) of OCs may increase the risk of diabetes among Chinese women. However, the attributable risk for diabetes among OC users in the general population, if confirmed by further studies, appears to be small.

PMID: 14969675 [PubMed - in process]

15: Hum Reprod. 2004 Mar;19(3):741-56. Epub 2004 Jan 29.

Influence of HRT on prognostic factors for breast cancer: a systematic review after the Women's Health Initiative trial.

Antoine C, Liebens F, Carly B, Pastijn A, Rozenberg S; Women's Health Initiative.

INTRODUCTION: Mortality due to breast cancer has been reported to be the same or even lower in HRT users than in non-users. This has been attributed to earlier diagnosis and to better prognosis. Nevertheless, more advanced disease in HRT users was reported recently by the Women's Health Initiative (WHI) study. The objective of this study was to assess, using a systematic review of current literature, whether the data of the WHI study are in contradiction to observational data.

METHODS: We selected 25 studies, for which we evaluated the methodology, the characteristics of the studied populations, confounding breast cancer risk factors and prognostic indicators. **RESULTS:** The WHI study, showing a worsening of some prognostic parameters, is in contradiction to most published observational studies. Most observational studies are retrospective, not well matched and did not consider most confounding factors. Their methodology and selection criteria varied considerably and the number of patients was often small. No differences in the distributions of histology, grade or steroid receptors were observed in the WHI trial, while this was the case in some of the observational studies. Other parameters (S phase, protein Neu, Bcl-2 gene, protein p53 and E-cadherin, cathepsin D) were not reported in the WHI trial. **CONCLUSIONS:** In view of these data, the current clinical message to patients should be changed: one can no longer declare that breast cancers developed while using HRT are of better prognosis.

PMID: 14998980 [PubMed - in process]

16: Hypertension. 2004 Mar 15 [Epub ahead of print]

Novel Mechanisms Responsible for Postmenopausal Hypertension.

Reckelhoff JF, Fortepiani LA.

Blood pressure increases in many women after menopause. Hypertension is one of the major risk factors for cardiovascular disease. However, the mechanisms responsible for the postmenopausal increase in blood pressure are yet to be elucidated. Various humoral systems have been proposed to play a role in postmenopausal hypertension, such as changes in estrogen/androgen ratios,

increases in endothelin and oxidative stress, and activation of the renin-angiotensin system (RAS). In addition, obesity, type II diabetes, and activation of the sympathetic nervous system are common in postmenopausal women and may also play important roles. However, progress in elucidating the mechanisms responsible for postmenopausal hypertension has been hampered by the lack of a suitable animal model. The aging female spontaneously hypertensive rat (SHR) exhibits many of the characteristics found in postmenopausal women. In this review, some of the possible mechanisms that could play a role in postmenopausal hypertension are discussed, as well as the characteristics of the aged female SHR as a model to study.

PMID: 15023933 [PubMed - as supplied by publisher]

17: Int J Cancer. 2004 Mar 20;109(2):274-7.

Survival of cervix cancer patients in Harare, Zimbabwe, 1995-1997.

Chokunonga E, Ramanakumar AV, Nyakabau AM, Borok MZ, Chirenje ZM, Sankila R, Parkin DM.

The survival experience of 284 patients with cancer of the cervix uteri registered by the population-based Zimbabwe National Cancer Registry in 1995-1997 is described. The vital status of these subjects was established by linkage with death registration and by retrieval of patient files from medical records departments. Untraced patients were contacted at home. Of the 284, 177 (62.3%) were dead and 76 (26.8%) were alive at the closing date of the study (31 December 1999), with only 31 cases (10.9%) lost to follow-up. Overall observed and relative survival at 3 years were 44.2% and 45.2%, respectively. Half of the cases (139) had been referred and treated in the radiotherapy department. Survival was significantly greater in the first 3 years for patients who received radiotherapy treatment compared to those that had not, but this difference had disappeared by the fourth year of follow-up. Many cases presented late (distant metastasis), and extent of disease was an important determinant of survival; cases with metastases had a risk of death some 3 times that of patients with localized disease. The results demonstrate the importance of earlier diagnosis and availability of effective treatment in the African context. Copyright 2003 Wiley-Liss, Inc.

PMID: 14750180 [PubMed - indexed for MEDLINE]

18: J Clin Oncol. 2004 Mar 15;22(6):1063-70.

Safety of treatment of metastatic breast cancer with trastuzumab beyond disease progression.

Tripathy D, Slamon DJ, Cobleigh M, Arnold A, Saleh M, Mortimer JE, Murphy M, Stewart SJ.

PURPOSE: In a pivotal phase III trial, the addition of trastuzumab to chemotherapy significantly improved response rate, time to disease progression, and overall survival in women with HER2 overexpressing metastatic breast cancer. We conducted an extension study to this trial to obtain additional safety information and to provide trastuzumab following disease progression. **PATIENTS AND METHODS:** A total of 247 patients with documented disease progression received weekly intravenous trastuzumab in the extension study. Concurrent therapies were administered at the discretion of the treating physician. Patient groups were based on initial study treatment: chemotherapy alone (group 1, n=154) or chemotherapy plus trastuzumab (group 2, n=93). **RESULTS:** Sixty-eight percent of group 1 and 76% of group 2 received chemotherapy plus trastuzumab in the extension trial; the remainder received trastuzumab alone or combined with palliative radiotherapy or hormonal therapy. Seventy-six percent of group 1 and 55% of group 2 experienced

at least one adverse event, similar to effects observed in the pivotal trial. Symptomatic or asymptomatic cardiac dysfunction occurred in 9% of group 1 and 2% of group 2 patients. Overall objective response rates were 14% in group 1 and 11% in group 2; median durations of response exceeded 6 months in both groups. **CONCLUSION:** Our results suggest that prolonged use of trastuzumab therapy is safe and well tolerated. Longer durations of therapy did not appear to increase the risk of cardiac dysfunction. Patients progressing on trastuzumab-containing therapy demonstrate some response to a second trastuzumab-containing regimen. The independent contribution of trastuzumab in this setting merits further study.
PMID: 15020607 [PubMed - in process]

19: J Midwifery Womens Health. 2004 Mar-Apr;49(2):169-170.
A home study program sponsored by JMWH: managing menopausal symptoms after the women's health initiative (#2003/103).
[No authors listed]
PMID: 15010682 [PubMed - as supplied by publisher]

20: J Midwifery Womens Health. 2004 Mar-Apr;49(2):87-95.
CEU:Managing menopausal symptoms after the women's health initiative.
Hackley B, Rousseau ME. barbara.hackley@yale.edu

Until the results of the Women's Health Initiative (WHI) were released in July 2002, hormone replacement therapy (HRT) had been thought to be the most effective way to manage unwanted menopausal symptoms and to prevent long-term health problems associated with aging. The results of the WHI, showing that HRT is less beneficial and associated with more risks than previously thought, has complicated the management of unwanted menopausal symptoms. This article discusses the effectiveness of HRT and other modalities used to relieve menopausal symptoms and discusses how to choose an HRT product to match specific menopausal complaints and provide maximum safety.
PMID: 15010660 [PubMed - in process]

21: J Natl Cancer Inst. 2004 Mar 3;96(5):403-7.
Heme iron, zinc, alcohol consumption, and colon cancer: Iowa Women's Health Study.
Lee DH, Anderson KE, Harnack LJ, Folsom AR, Jacobs DR Jr.

We examined associations among colon cancer incidence and dietary intake of heme iron, a possible prooxidant, zinc, a possible antioxidant, and alcohol, a disruptor of iron homeostasis. During 15 years of follow-up, 34 708 postmenopausal women, aged 55-69 years at baseline who completed a food-frequency questionnaire for the Iowa Women's Health Study, were followed for incident colon cancer. After adjusting for each micronutrient, the relative risks for proximal colon cancer increased more than twofold across categories of heme iron intake (P(trend) =.01) and the corresponding relative risks decreased more than 50% across categories for zinc intake (P(trend) =.01). The positive association with heme iron and the inverse association with zinc intake were stronger among women who consumed alcohol than among those who did not. Zinc intake was also associated with a decreased risk of distal colon cancer (P(trend) =.03), regardless of alcohol or heme iron consumption. Our results suggest that intake of dietary heme iron is associated with an increased risk of proximal colon cancer, especially among women who drink, but that intake of dietary zinc is associated with a decreased risk of both proximal and distal colon cancer.
PMID: 14996862 [PubMed - indexed for MEDLINE]

22: J Natl Cancer Inst. 2004 Mar 3;96(5):347-8.

Canadian society takes position on long-term hormone therapy.

Smith M.

PMID: 14996851 [PubMed - indexed for MEDLINE]

23: JAMA. 2004 Mar 10;291(10):1220-5.

Sex differences in outcomes after cardiac catheterization: effect modification by treatment strategy and time.

King KM, Ghali WA, Faris PD, Curtis MJ, Galbraith PD, Graham MM, Knudtson ML.

CONTEXT: Studies comparing outcomes of cardiac care in women vs men yield various results, with some suggesting worse outcomes for women and others suggesting equivalent outcomes. OBJECTIVE: To determine whether extent of coronary disease, treatment strategy, and follow-up time influence the risk of death in women vs men among patients who have had cardiac catheterization. DESIGN, SETTING, AND PATIENTS: We studied a large inception cohort by using detailed clinical data from a registry of 37 401 patients undergoing cardiac catheterization in Alberta, Canada, from 1995-2000, with follow-up through December 31, 2001. MAIN OUTCOME MEASURES: The risk of death for women vs men was assessed for all patients combined and then in analyses stratified by degree of coronary anatomic risk and by treatment strategy (no revascularization, percutaneous coronary intervention [PCI], coronary artery bypass graft [CABG] surgery). The latter analysis included a graphic assessment of the changing relative risk over time for women vs men. RESULTS: Women had higher 1-year mortality than men did (5.6% vs 4.6%; $P < .001$). However, stratified analyses demonstrated that sex differences in risk occurred only early after catheterization and were most apparent among patients undergoing revascularization. The early risk-adjusted relative risks for women vs men were elevated at 3.49 (95% confidence interval [CI], 1.95-6.24) for CABG surgery and 2.38 (95% CI, 1.48-3.83) for PCI on day 1 after catheterization, with a subsequent decrease in relative risk over time to equivalence in risk between sexes before 1 year. CONCLUSIONS: Sex-based differences in death rates after cardiac catheterization are time- and treatment-specific. This finding may at least partially explain the discrepancies in results from earlier studies on sex differences in outcomes of cardiac care.

PMID: 15010443 [PubMed - indexed for MEDLINE]

24: N Engl J Med. 2004 Mar 11;350(11):1104-10.

Comment in: N Engl J Med. 2004 Mar 11;350(11):1073-5.

Calcitonin gene-related peptide receptor antagonist BIBN 4096 BS for the acute treatment of migraine.

Olesen J, Diener HC, Husstedt IW, Goadsby PJ, Hall D, Meier U, Pollentier S, Lesko LM; BIBN 4096 BS Clinical Proof of Concept Study Group.

BACKGROUND: Calcitonin gene-related peptide (CGRP) may have a causative role in migraine. We therefore hypothesized that a CGRP-receptor antagonist might be effective in the treatment of migraine attacks. METHODS: In an international, multicenter, double-blind, randomized clinical trial of BIBN 4096 BS, a highly specific and potent nonpeptide CGRP-receptor antagonist, 126 patients with migraine received one of the following: placebo or 0.25, 0.5, 1, 2.5, 5, or 10 mg of BIBN 4096 BS intravenously over a period of 10 minutes. A group-sequential adaptive treatment-assignment design was used to minimize the number of patients exposed. RESULTS: The 2.5-mg dose was selected, with a response rate of 66 percent, as compared with 27 percent for placebo ($P = 0.001$). The BIBN 4096 BS group as a whole had a response rate of 60 percent. Significant superiority over placebo was

also observed with respect to most secondary end points: the pain-free rate at 2 hours; the rate of sustained response over a period of 24 hours; the rate of recurrence of headache; improvement in nausea, photophobia, phonophobia, and functional capacity; and the time to meaningful relief. An effect was apparent after 30 minutes and increased over the next few hours. The overall rate of adverse events was 25 percent after the 2.5-mg dose of the drug and 20 percent for the BIBN 4096 BS group as a whole, as compared with 12 percent for placebo. The most frequent side effect was paresthesia. There were no serious adverse events. **CONCLUSIONS:** The CGRP antagonist BIBN 4096 BS was effective in treating acute attacks of migraine. Copyright 2004 Massachusetts Medical Society
PMID: 15014183 [PubMed - indexed for MEDLINE]

25: N Engl J Med. 2004 Mar 11;350(11):1073-5.

Comment on: N Engl J Med. 2004 Mar 11;350(11):1104-10.

CGRP-receptor antagonists--a fresh approach to migraine therapy?

Durham PL.

PMID: 15014178 [PubMed - indexed for MEDLINE]

26: N Engl J Med. 2004 Mar 11;350(11):1081-92.

Comment in: N Engl J Med. 2004 Mar 11;350(11):1140-2.

A randomized trial of exemestane after two to three years of tamoxifen therapy in postmenopausal women with primary breast cancer.

Coombes RC, Hall E, Gibson LJ, Paridaens R, Jassem J, Delozier T, Jones SE, Alvarez I, Bertelli G, Ortmann O, Coates AS, Bajetta E, Dodwell D, Coleman RE, Fallowfield LJ, Mickiewicz E, Andersen J, Lonning PE, Cocconi G, Stewart A, Stuart N, Snowdon CF, Carpentieri M, Massimini G, Bliss JM; Intergroup Exemestane Study.

BACKGROUND: Tamoxifen, taken for five years, is the standard adjuvant treatment for postmenopausal women with primary, estrogen-receptor-positive breast cancer. Despite this treatment, however, some patients have a relapse. **METHODS:** We conducted a double-blind, randomized trial to test whether, after two to three years of tamoxifen therapy, switching to exemestane was more effective than continuing tamoxifen therapy for the remainder of the five years of treatment. The primary end point was disease-free survival. **RESULTS:** Of the 4742 patients enrolled, 2362 were randomly assigned to switch to exemestane, and 2380 to continue to receive tamoxifen. After a median follow-up of 30.6 months, 449 first events (local or metastatic recurrence, contralateral breast cancer, or death) were reported--183 in the exemestane group and 266 in the tamoxifen group. The unadjusted hazard ratio in the exemestane group as compared with the tamoxifen group was 0.68 (95 percent confidence interval, 0.56 to 0.82; $P < 0.001$ by the log-rank test), representing a 32 percent reduction in risk and corresponding to an absolute benefit in terms of disease-free survival of 4.7 percent (95 percent confidence interval, 2.6 to 6.8) at three years after randomization. Overall survival was not significantly different in the two groups, with 93 deaths occurring in the exemestane group and 106 in the tamoxifen group. Severe toxic effects of exemestane were rare. Contralateral breast cancer occurred in 20 patients in the tamoxifen group and 9 in the exemestane group ($P = 0.04$). **CONCLUSIONS:** Exemestane therapy after two to three years of tamoxifen therapy significantly improved disease-free survival as compared with the standard five years of tamoxifen treatment. Copyright 2004 Massachusetts Medical Society

PMID: 15014181 [PubMed - indexed for MEDLINE]

27: N Engl J Med. 2004 Mar 4;350(10):991-1004.

Estrogen plus progestin and colorectal cancer in postmenopausal women.

Chlebowski RT, Wactawski-Wende J, Ritenbaugh C, Hubbell FA, Ascensao J, Rodabough RJ, Rosenberg CA, Taylor VM, Harris R, Chen C, Adams-Campbell LL, White E; Women's Health Initiative Investigators.

BACKGROUND: Although the Women's Health Initiative (WHI) trial of estrogen plus progestin in postmenopausal women identified more overall health risks than benefits among women in the hormone group, the use of estrogen plus progestin was associated with a significant decrease in the risk of colorectal cancer. We analyzed features of the colorectal cancers that developed and their relation to the characteristics of the participants. **METHODS:** In the WHI trial, 16,608 postmenopausal women who were 50 to 79 years of age and had an intact uterus were randomly assigned to a combination of conjugated equine estrogens (0.625 mg per day) plus medroxyprogesterone acetate (2.5 mg per day) or placebo. The main outcome measures were the incidence, stages, and types of colorectal cancer, as determined by blinded central adjudication. **RESULTS:** There were 43 invasive colorectal cancers in the hormone group and 72 in the placebo group (hazard ratio, 0.56; 95 percent confidence interval, 0.38 to 0.81; P=0.003). The invasive colorectal cancers in the hormone group were similar in histologic features and grade to those in the placebo group but with a greater number of positive lymph nodes (mean +/-SD, 3.2+/-4.1 vs. 0.8+/-1.7; P=0.002) and were more advanced (regional or metastatic disease, 76.2 percent vs. 48.5 percent; P=0.004). In exploratory analyses, women in the hormone group with antecedent vaginal bleeding had colorectal cancers with a greater number of positive nodes than women in the hormone group who did not have vaginal bleeding (3.8+/-4.3 vs. 0.7+/-1.5 nodes, P=0.006). **CONCLUSIONS:** Relatively short-term use of estrogen plus progestin was associated with a decreased risk of colorectal cancer. However, colorectal cancers in women who took estrogen plus progestin were diagnosed at a more advanced stage than those in women who took placebo. Copyright 2004 Massachusetts Medical Society

PMID: 14999111 [PubMed - indexed for MEDLINE]

28: Neurology. 2004 Mar 9;62(5):811-4.

Association of APOE polymorphisms with disease severity in MS is limited to women.

Kantarci OH, Hebrink DD, Achenbach SJ, Pittock SJ, Altintas A, Schaefer-Klein JL, Atkinson EJ, De Andrade M, McMurray CT, Rodriguez M, Weinshenker BG.

The authors studied the association of an exon 4 (E4*epsilon2/3/4) and three promoter polymorphisms of APOE with disease course and severity stratified by gender in 221 patients with multiple sclerosis from two overlapping population-based prevalence cohorts. Women carriers of the E4*epsilon2 allele took longer to attain an Expanded Disability Status Scale score of 6 (p = 0.015) and had more favorable ranked severity scores than noncarriers (p = 0.009). There was no association in men. Alleles epsilon3 or epsilon4 and promoter polymorphisms were not associated with disease course or severity.

PMID: 15007140 [PubMed - in process]

29: Obstet Gynecol. 2004 Mar;103(3):440-6.

Rapid loss of hip fracture protection after estrogen cessation: evidence from the National Osteoporosis Risk Assessment.

Yates J, Barrett-Connor E, Barlas S, Chen YT, Miller PD, Siris ES.

OBJECTIVE: Since the findings from the Women's Health Initiative became available in July 2002, millions of women have discontinued postmenopausal hormone therapy (HT). The objective of this study was to evaluate the association between HT

cessation and hip fracture risk. **METHODS:** Women who participated in the National Osteoporosis Risk Assessment and completed the 12-month follow-up survey were studied. All participants were aged at least 50 years, were postmenopausal, and had no previous diagnosis of osteoporosis. Baseline and 12-month follow-up questionnaires assessed use of HT and incident fractures. Of the 140,584 women in this study, 269 reported an incident hip fracture. A logistic regression model was used to assess association between HT use and incident hip fracture, controlling for potential confounders. **RESULTS:** Consistent with the Women's Health Initiative, women in National Osteoporosis Risk Assessment who were currently on HT had a 40% lower incidence of hip fractures compared with those who never used HT. Women who stopped using HT more than 5 years earlier had similar hip fracture risk to never users, as expected. However, surprisingly, women who had discontinued HT within the previous 5 years had an increased hip fracture odds ratio of 1.65 (95% confidence interval 1.05, 2.59) relative to never users of HT. **CONCLUSION:** Postmenopausal women who have discontinued HT within the past 5 years have a risk for hip fracture that is at least as high as that in women who have never used HT. **LEVEL OF EVIDENCE:** II-2
PMID: 14990403 [PubMed - in process]

30: Oncol Nurs Forum. 2004 Mar-Apr;31(2):249-63.

Continuing education: risks and benefits of soy isoflavones for breast cancer survivors.

Hu SA.

PURPOSE/OBJECTIVES: To present state-of-the-art information about the risks and benefits of soy isoflavones for breast cancer survivors. **DATA SOURCES:** Published research articles, pertinent articles and books, and computerized databases. **DATA SYNTHESIS:** Some epidemiologic data suggest that soy isoflavones play an important role in preventing breast cancer in Asian women and promoting women's health in a variety of ways. However, the use of soy isoflavones in women with breast cancer is controversial. Risks and benefits exist regarding the use of soy isoflavones by breast cancer survivors. **CONCLUSIONS:** The use of soy isoflavones to promote health in breast cancer survivors remains controversial because of scant scientific data. **IMPLICATIONS FOR NURSING:** Nurses should not only provide updated information to the public but also interpret research results carefully. More clinical trials need to be conducted on a longitudinal basis with the enrollment of breast cancer survivors.

PMID: 15017441 [PubMed - in process]