

Test Required for Laparoscopy Privileges in Boston

BY JANE ANDERSON
Contributing Writer

In a move that sponsors believe is the first of its kind in the United States, attending general surgeons at several Boston-area hospitals will be required to prove basic motor skills outside an operating room before obtaining laparoscopic surgery privileges.

And as an incentive toward completion of the Fundamentals in Laparoscopic

Surgery (FLS) exam, CRICO/RMF, the Harvard medical community’s professional liability insurer, is providing a one-time \$500 patient safety incentive to general surgeons who pass the exam.

The new requirement—which is going into effect at Beth Israel Deaconess Medical Center, Cambridge Health Alliance, and Massachusetts General Hospital, all of which are in Boston—could portend adoption of the FLS standards in many hospitals, said Dr. Steven Schwartzberg, chief of

surgery at the Cambridge Health Alliance.

“I expect it to spread,” Dr. Schwartzberg said in an interview. “I think this is going to become quite viral in terms of its impact and rate of spread, and pick up dramatically.”

The FLS program, which includes hands-on skills training and assessment tools, took almost a decade to develop, and is a joint educational offering of the American College of Surgeons and the Society of Gastrointestinal and Endoscopic Surgeons.

The test is a two-part, proctored 75-question multiple choice exam administered by computer, plus an evaluation of skills based on speed and accuracy of the surgeon’s maneuvers using the FLS Laparoscopic Trainer Box.

The skills test consists of five nonprocedure-specific simulation exercises incorporating most of the psychomotor skills necessary for basic laparoscopic surgery. Surgeons are tested on their proficiency at suturing, cutting in a circle, and moving objects from one location to another.

Beth Israel Deaconess was the first U.S. hospital to require general surgeons performing laparoscopic surgery to pass the FLS exam, said Dr. Daniel Jones, the hospital’s chief of minimally invasive surgery.

The hospital started requiring residents to prove competency in laparoscopy about 10 years ago, Dr. Jones said in an interview. “Finally we said: Why should we hold trainees to a higher level than surgeons in practice? Would you let a truck driver drive after only a written exam?”

Dr. Jones said surgeons can elect to simply take the test without taking the course first. “I did that,” he said. “But it’s a real test, and it’s better to study and practice first. It’s nothing less than a patient would expect their surgeon to do effortlessly.”

In the Boston area, professional liability insurer CRICO/RMF sponsored the FLS course in January, and about 60 people signed up, said Dr. Schwartzberg. Beth Israel Deaconess and Cambridge Health Alliance have already adopted the FLS exam as a requirement for laparoscopic privileges, and Massachusetts General Hospital will do so in the near future, said Dr. David Rattner, chief of the division of general and gastrointestinal surgery at Massachusetts General.

Surgeons insured by CRICO/RMF who pass the exam will receive a one-time \$500 patient safety incentive from the insurer, as well as continuing medical education credits through SAGES and ACS. But “it’s not about the money,” said Dr. Jones. “It’s about sending the signal that the bar has been raised.”

Dr. Jones said he expects the FLS to become the new minimal standard for all surgeons offering basic laparoscopy to patients. And Dr. Schwartzberg agreed, saying the FLS, like the Advanced Trauma Life Support (ATLS) curriculum in trauma surgery, indicates a move toward more testing of skills and competency in surgery in general.

“You wouldn’t work in a trauma [emergency department] without the ATLS,” said Dr. Schwartzberg. “Will this be a model for other aspects of surgery? I think so.”

ENJUVIA™
(synthetic conjugated estrogens, 0.625 mg tablets)
(Rx only)
Brief Summary (See package brochure for full prescribing information)

ESTROGENS INCREASE THE RISK OF ENDOMETRIAL CANCER
Close clinical surveillance of all women taking estrogen is important. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. There is no evidence that the use of natural estrogens results in a different endometrial risk profile than synthetic estrogens of equivalent estrogen doses. (See **WARNINGS: Malignant neoplasms, Endometrial cancer.**)

CARDIOVASCULAR AND OTHER RISKS Estrogens with or without progestins should not be used for the prevention of cardiovascular disease or dementia. (See **CLINICAL STUDIES AND WARNINGS: Cardiovascular disorders and Dementia.**) The estrogen alone subcategory of the Women’s Health Initiative (WHI) reported increased risks of stroke and deep vein thromboses (DVT) in postmenopausal women (50 to 79 years of age) during 6.8 years and 7.1 years, respectively, of treatment with oral conjugated estrogens (CE 0.625 mg) alone per day, relative to placebo. (See **CLINICAL STUDIES AND WARNINGS: Cardiovascular disorders.**) The estrogen-plus-progestin subcategory of the WHI reported increased risks of myocardial infarction, stroke, invasive breast cancer, pulmonary emboli, and deep vein thromboses in postmenopausal women (50 to 79 years of age) during 3.6 years of treatment with oral conjugated estrogens (CE 0.625 mg) combined with medroxyprogesterone acetate (MPA 2.5 mg) per day, relative to placebo. (See **CLINICAL STUDIES AND WARNINGS: Cardiovascular disorders and Malignant neoplasms.**)

Breast cancer: The Women’s Health Initiative Memory Study (WHIMS), a substudy of the WHI study, reported an increased risk of developing probable dementia in postmenopausal women 65 years of age or older during 5.2 years of treatment with CE 0.625 mg alone and during 4 years of treatment with CE 0.625 mg combined with MPA 2.5 mg, relative to placebo. It is unknown whether this finding applies to younger postmenopausal women. (See **CLINICAL STUDIES, WARNINGS, Dementia and PRECAUTIONS, Geriatric Use.**) Other doses of conjugated estrogens and medroxyprogesterone acetate, and other combinations and dosage forms of estrogens and progestins, were not studied in the WHI clinical trials, and in the absence of comparable data, these risks should be assumed to be similar. Because of these risks, estrogens with or without progestins should be prescribed at the lowest effective doses and for the shortest duration consistent with treatment goals and risks for the individual woman.

CONTRAINDICATIONS: ENJUVIA tablets should not be used in women with any of the following conditions: 1. Undiagnosed abnormal genital bleeding. 2. Known, suspected, or history of cancer of the breast. 3. Known or suspected estrogen-dependent neoplasia. 4. Active deep vein thromboses, pulmonary embolism, or a history of these conditions. 5. Active or recent (i.e., within the past year) arterial thromboembolic disease (e.g., stroke, myocardial infarction). 6. Liver dysfunction or disease. 7. Known hypersensitivity to the ingredients of ENJUVIA tablets. 8. Known or suspected pregnancy. There is no indication for ENJUVIA in pregnancy. There appears to be little or no increase in risk of birth defects in children born to women who have used estrogens and progestins from oral contraceptives inadvertently during early pregnancy. (See **PRECAUTIONS, Fertility.**)

WARNINGS: See BOXED WARNING. 1. **Cardiovascular disorders:** Estrogen and estrogen-progestin therapies have been associated with an increased risk of cardiovascular events such as myocardial infarction and stroke, as well as venous thromboses and pulmonary embolism (venous thromboembolism [VTE]). Should any of these occur or be suspected, estrogens should be discontinued immediately. Risk factors for arterial vascular disease (e.g., hypertension, diabetes mellitus, tobacco use, hypercholesterolemia, and obesity) and/or venous thromboembolism (e.g., personal history or family history of VTE, obesity, and systemic lupus erythematosus) should be managed appropriately. **2. Stroke:** In the estrogen-alone subcategory of the Women’s Health Initiative (WHI) study, statistically significant increased risk of stroke was reported in women receiving CE 0.625 mg daily compared to women receiving placebo (44 versus 32 per 10,000 women-years). The increase in risk was demonstrated in year 1 and persisted. (See **CLINICAL STUDIES.**) In the estrogen-plus-progestin subcategory of the WHI study, a statistically significant increased risk of stroke was reported in women receiving CE/MPA 0.625 mg/2.5 mg daily compared to women receiving placebo (51 vs. 24 per 10,000 women-years). The increase in risk was demonstrated after the first year and persisted. (See **CLINICAL PHARMACOLOGY, Clinical Studies.**) **3. Coronary heart disease:** In the estrogen-alone subcategory of the WHI study, no overall effect on coronary heart disease (CHD) events (defined as non-fatal CHD, fatal CHD, and overall CHD) was reported in women receiving estrogen alone compared to placebo. (See **CLINICAL STUDIES.**) In the estrogen-plus-progestin subcategory of the WHI study, no statistically significant increase of CHD events was reported in women receiving CE/MPA compared to women receiving placebo (29 versus 33 per 10,000 women-years). An increase in relative risk was demonstrated in year 1, and a trend toward decreasing relative risk was reported in years 2 through 5. In postmenopausal women with documented heart disease (n = 2,763; average age 66.7 years), a controlled clinical trial of secondary prevention of cardiovascular disease (Heart and Estrogen/Progestin Replacement Study [HERS]) treatment with CE/MPA (0.625 mg/2.5 mg per day) demonstrated no cardiovascular benefit. During an average follow-up of 4.1 years, treatment with CE/MPA did not reduce the overall rate of CHD events in postmenopausal women with established coronary heart disease. There were more CHD events in the CE/MPA treated group than in the placebo group in year 1, but not during the subsequent years. Participation in an open label extension of the original HERS trial (HERS II) was agreed to by 2,321 women. Average follow-up in HERS II was an additional 2.7 years, for a total of 6.8 years of follow-up. Relative to overall events comparable among women in the CE/MPA group and the placebo group in HERS, HERS II and overall, larger doses of conjugated estrogens per day, compared to those used to treat cancer of the prostate and breast, have been shown in a large prospective clinical trial to increase the risks of nonfatal myocardial infarction, pulmonary embolism, and thromboembolism. **4. Venous thromboembolism:** In the estrogen-alone subcategory of the WHI study, the risk of VTE (DVT and pulmonary embolism [PE]) was reported to be increased for women taking conjugated equine estrogens (30 vs. 22 per 10,000 women-years), although only the increased risk of DVT reached statistical significance (23 vs. 13 per 10,000 women-years). The increase in VTE risk was demonstrated during the first year. (See **CLINICAL STUDIES.**) In the estrogen-plus-progestin subcategory of the WHI study, a statistically significant 2-fold greater rate of VTE was reported in women receiving CE/MPA compared to women receiving placebo (33 vs. 17 per 10,000 women-years). Statistically significant increases in risk for both DVT (26 vs. 13 per 10,000 women-years) and PE (18 vs. 6 per 10,000 women-years) were also demonstrated. The increase in VTE risk was demonstrated during the first year and persisted. If feasible, estrogens should be discontinued at least 4 to 6 weeks before surgery of the type associated with an increased risk of thromboembolism, or during periods of prolonged immobilization. **5. Malignant neoplasms: Endometrial cancer:** The use of unopposed estrogens in women with intact uterus has been associated with an increased risk of endometrial cancer. The reported endometrial cancer risk among unopposed estrogen users is about 2- to 12-times greater than in non-users, and appears dependent on duration of treatment and on estrogen dose. Most studies show no significant increased risk associated with use of estrogens for less than 1 year. The greatest risk appears associated with prolonged use, with increased risks of 15- to 24-fold for 5 to 10 years or more. This risk has been shown to persist for at least 1 to 15 years after estrogen therapy is discontinued. Clinical surveillance of all women taking estrogen-progestin combinations is important. Adequate diagnostic measures, including endometrial sampling when indicated, should be undertaken to rule out malignancy in all cases of undiagnosed persistent or recurring abnormal vaginal bleeding. There is no evidence that the use of natural estrogens results in a different endometrial risk profile than synthetic estrogens of equivalent estrogen doses. Adding a progestin to estrogen therapy has been shown to reduce the risk of endometrial hyperplasia, which may be a precursor to endometrial cancer. **6. Breast cancer:** In some studies, the use of estrogens and progestins by postmenopausal women has been reported to increase the risk of breast cancer. The most important randomized clinical trial providing information about this issue is the Women’s Health Initiative Adjuvant Breast and Bowel (ABT) trial. The results from observational studies are generally consistent with those of the WHI clinical trial. Observational studies have also reported an increased risk of breast cancer for estrogen-plus-progestin combination therapy, and a smaller increased risk for estrogen-alone therapy, after several years of use. For both findings, the excess risk increased with duration of use, and appeared to return to baseline over about five years after stopping treatment (only the observational studies have substantial data on risk after stopping). In these studies, the risk of breast cancer was greater, and became apparent earlier, with estrogen-plus-progestin combination therapy as compared to estrogen-alone therapy. However, these studies have not found significant variation in the risk of breast cancer among different estrogens or among different estrogen-plus-progestin combinations, doses, or regimens of administration. In the estrogen-alone subcategory of the WHI trial, after an average of 7.1 years of follow-up, CE 0.625 mg daily was not associated with an increased risk of invasive breast cancer (RR 0.86, 95% CI 0.62-1.04). In the estrogen-plus-progestin subcategory, after a mean follow-up of 3.6 years, the WHI study reported an increased risk of breast cancer. In this subcategory, prior use of estrogen alone or estrogen-plus-progestin combination hormone therapy was reported by 20% of the women. The relative risk of invasive breast cancer was 1.24 (95% CI 1.01-1.54), and the absolute risk was 41 vs. 33 cases per 10,000 women-years. For estrogen plus progestin compared with placebo, respectively, 49.3 women who reported prior use of hormone therapy, the relative risk of invasive breast cancer was 1.88, and the absolute risk was 46 vs. 25 cases per 10,000 women-years, for estrogen plus progestin compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.00, and the absolute risk was 40 vs. 38 cases per 10,000 women-years for estrogen plus progestin compared with placebo. In the WHI trial, invasive breast cancers were larger and diagnosed at a more advanced stage in the estrogen-plus-progestin group compared with the placebo group. Metastatic disease was rare, with no apparent difference between the two groups. Other prognostic factors, such as histologic subtype, grade and hormone receptor status did not differ between the groups. The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. All women should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. In addition, mammography examinations should be scheduled based on patient age, risk factors, and prior mammogram results. **8. Dementia:** In the estrogen-alone Women’s Health Initiative Memory Study (WHIMS), a substudy of the WHI study, a population of 2,947 postmenopausal women aged 65 to 79 years was randomized to CE 0.625 mg daily or placebo. In the estrogen-plus-progestin WHIMS subcategory, a population of 4,532 postmenopausal women aged 65 to 79 years was randomized to CE/MPA (0.625 mg/2.5 mg) daily or placebo. In the estrogen-alone subcategory, after an average follow-up of 6.2 years, 28 women in the estrogen-alone group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE alone vs. placebo was 1.49 (95% CI 0.83-2.66). The absolute risk of probable dementia for CE alone vs. placebo was 37 vs. 25 cases per 10,000 women-years. In the estrogen-plus-progestin subcategory, after an average follow-up of four years, 40 women in the estrogen-plus-progestin group and 21 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE/MPA vs. placebo was 2.25 (95% CI 1.21-3.48). The absolute risk of probable dementia for CE/MPA vs. placebo was 45 vs. 22 cases per 10,000 women-years. When data from the two populations were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.78 (95% CI 1.19-2.68). Since both substudies were conducted in women aged 65 to 79 years, it is unknown whether these findings apply to younger postmenopausal women. (See **BOXED WARNING, WARNINGS, Dementia.**) **ADVERSE REACTIONS:** See **BOXED WARNINGS, WARNINGS and PRECAUTIONS.** Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. The adverse reaction information from clinical trials does, however, provide a basis for identifying the adverse events that appear to be related to drug use and for approximating rates. In a 12-week clinical trial, 208 postmenopausal women with vasomotor symptoms were treated with ENJUVIA. Adverse events that occurred at a rate greater than or equal to 5% and greater than placebo, regardless of whether drug is discontinued, or during vasomotor events, are listed below. **Body as a Whole:** Abdominal Pain, Abdominal Pain (Upper), Pain, Back Pain. **Cardiovascular System:** Edema, Hypertension, Hypotension, Contact Intense. **7. Central Nervous System:** Headache, Migraine, Dizziness, Mental Discomfort, Chorea, Nervousness, Mood Disturbance, Irritability, Exacerbation of epilepsy, dementia. **8. Musculoskeletal:** Increase or decrease in weight, reduced carbohydrate tolerance, aggravation of porphyria, edema, arthralgia, leg cramps, changes in libido, urticaria, angioedema, angiofibrosarcoma-like reactions, hypocalcemia, exacerbation of asthma, increased triglycerids, increased APTT. 2007 - 85-406, 407, 408, 420, 410

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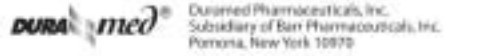
Enjuvia
(synthetic conjugated estrogens, 0.625 mg tablets)

WARNINGS AND PRECAUTIONS: See boxed warnings, warnings and precautions. Estrogens in certain animal species increase the frequency of condyroma of the breast, uterine, cervical, vaginal, and liver. **F. Pregnancy:** ENJUVIA tablets should not be used during pregnancy. (See **CONTRAINDICATIONS**.) **G. Nursing Mothers:** Estrogen administration to nursing mothers has been shown to decrease the quantity and quality of the milk. Detectable amounts of estrogens have been identified in the milk of mothers receiving this drug. Caution should be exercised when ENJUVIA is administered to a nursing woman. **H. Pediatric Use:** The safety and efficacy of ENJUVIA tablets in pediatric patients has not been established. **I. Geriatric Use:** Clinical studies of ENJUVIA did not include sufficient numbers of subjects aged 65 and over to determine whether they respond differently than younger subjects. Of the total number of subjects in the estrogen-alone subcategory of the WHI study, 46 percent (n = 4,945) were 65 years and older, while 7.7 percent (n = 757) were 75 years and older. There was a higher relative risk (CE versus placebo) of stroke in women less than 75 years of age compared to women 75 years and older. In the estrogen-alone subcategory of the WHI study, a population of 2,947 postmenopausal women aged 65 to 79 years was randomized to CE 0.625 mg daily or placebo. After an average follow-up of 6.2 years, 28 women in the CE group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE alone vs. placebo was 1.49 (95% CI 0.83-2.66). The absolute risk of probable dementia for CE alone vs. placebo was 37 vs. 25 cases per 10,000 women-years. In the estrogen-plus-progestin subcategory of the WHI study, a population of 4,532 postmenopausal women aged 65 to 79 years was randomized to CE/MPA (0.625 mg/2.5 mg) daily or placebo. In the estrogen-plus-progestin subcategory, after an average follow-up of four years, 40 women in the estrogen-plus-progestin group and 21 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE/MPA vs. placebo was 2.25 (95% CI 1.21-3.48). The absolute risk of probable dementia for CE/MPA vs. placebo was 45 vs. 22 cases per 10,000 women-years. When data from the two populations were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.78 (95% CI 1.19-2.68). Since both substudies were conducted in women aged 65 to 79 years, it is unknown whether these findings apply to younger postmenopausal women. (See **BOXED WARNING, WARNINGS, Dementia.**)

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In this subcategory, prior use of estrogen alone or estrogen-plus-progestin combination hormone therapy was reported by 20% of the women. The relative risk of invasive breast cancer was 1.24 (95% CI 1.01-1.54), and the absolute risk was 41 vs. 33 cases per 10,000 women-years. For estrogen plus progestin compared with placebo, respectively, 49.3 women who reported prior use of hormone therapy, the relative risk of invasive breast cancer was 1.88, and the absolute risk was 46 vs. 25 cases per 10,000 women-years, for estrogen plus progestin compared with placebo. Among women who reported no prior use of hormone therapy, the relative risk of invasive breast cancer was 1.00, and the absolute risk was 40 vs. 38 cases per 10,000 women-years for estrogen plus progestin compared with placebo. In the WHI trial, invasive breast cancers were larger and diagnosed at a more advanced stage in the estrogen-plus-progestin group compared with the placebo group. Metastatic disease was rare, with no apparent difference between the two groups. Other prognostic factors, such as histologic subtype, grade and hormone receptor status did not differ between the groups. The use of estrogen alone and estrogen plus progestin has been reported to result in an increase in abnormal mammograms requiring further evaluation. All women should receive yearly breast examinations by a healthcare provider and perform monthly breast self-examinations. In addition, mammography examinations should be scheduled based on patient age, risk factors, and prior mammogram results. **8. Dementia:** In the estrogen-alone Women’s Health Initiative Memory Study (WHIMS), a substudy of the WHI study, a population of 2,947 postmenopausal women aged 65 to 79 years was randomized to CE 0.625 mg daily or placebo. In the estrogen-plus-progestin WHIMS subcategory, a population of 4,532 postmenopausal women aged 65 to 79 years was randomized to CE/MPA (0.625 mg/2.5 mg) daily or placebo. In the estrogen-alone subcategory, after an average follow-up of 6.2 years, 28 women in the estrogen-alone group and 19 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE alone vs. placebo was 1.49 (95% CI 0.83-2.66). The absolute risk of probable dementia for CE alone vs. placebo was 37 vs. 25 cases per 10,000 women-years. In the estrogen-plus-progestin subcategory, after an average follow-up of four years, 40 women in the estrogen-plus-progestin group and 21 women in the placebo group were diagnosed with probable dementia. The relative risk of probable dementia for CE/MPA vs. placebo was 2.25 (95% CI 1.21-3.48). The absolute risk of probable dementia for CE/MPA vs. placebo was 45 vs. 22 cases per 10,000 women-years. When data from the two populations were pooled as planned in the WHIMS protocol, the reported overall relative risk for probable dementia was 1.78 (95% CI 1.19-2.68). Since both substudies were conducted in women aged 65 to 79 years, it is unknown whether these findings apply to younger postmenopausal women. (See **BOXED WARNING, WARNINGS, Dementia.**)



Dura Med Pharmaceuticals, Inc.
Subsidiary of Barr Pharmaceuticals, Inc.
Pomona, New York 10970