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CME

Detection of Fetal Anomalies with Routine Ultrasound

ABSTRACT & COMMENTARY

To determine how effectively routine ultrasound and other prenatal diagnostic techniques identify fetal malformations, Boyd and associates reviewed the experience at the Oxford Women's Centre in Great Britain between 1991 and 1996. Data for the study were derived from a registry of congenital malformations including chromosomal abnormalities diagnosed clinically or pathologically in all livebirths, neonatal deaths, stillbirths, and induced and spontaneous abortions delivered at the center. Of 33,376 babies, 725 (2%) were judged to be abnormal at birth. An anomaly scan at 18-22 weeks gestation was available to all the women, and approximately 90% had this study. While alpha-fetoprotein screening for neural tube defects was performed routinely, neither triple marker screening nor nuchal translucency screening has been done at Oxford.

More than half of the malformed fetuses and infants (n = 396, 55%) were correctly identified before delivery. The rate of detection improved over the six years of the study—from 42% in the first three years to 68% for the second three years. In 174 fetuses, an abnormality was suspected on ultrasound but the fetus was subsequently found to be normal. In more than 90% of these cases (n = 160, 92%), the false-positive result was due to the observation of a "soft" ultrasound marker, nuchal thickening, choroid plexus cysts, and echogenic bowel. These soft markers were responsible for a 4% increase in the detection rate of anomalies. These markers were also responsible for a 12-fold increase in false-positives, from 1/2332 to 1/188.

Boyd et al conclude that more than half of all malformed fetuses can be prenatally detected in routine practice, most after an abnormal ultrasound at 18-22 weeks gestation. The use of soft markers significantly increases the rate of false-positives and could result in greater parental anxiety. (Boyd PA, et al. *Lancet* 1998;352:1577-1581.)

COMMENT BY STEVEN G. GABBE, MD

The investigation describes the role of routine ultrasound in the prenatal diagnostic screening from a single center in Great Britain.

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INSIDE

While not a prospective, randomized trial, the size of the database (more than 33,000 cases) provides important information. This study, as have others, demonstrates that more than 50% of major fetal malformations can be detected by a routine ultrasound evaluation of fetal anatomy at 18-22 weeks gestation. It confirms that the detection rates for some malformations are significantly greater than for others. For isolated neural tube defects, the detection rate was highest—98%. For cardiac malformations, only 38% were recognized. Ultrasound proves to be far more important than other prenatal strategies, such as chromosome analysis for advanced maternal age or biochemical screening tests, in identifying fetal malformations. The information on the value of "soft" ultrasound markers is especially important. Of these variants of normal, nuchal thickening, and choroid plexus cyst, only one has a confirmed anomaly at delivery. Isolated nuchal thickening was seen in 78 pregnancies and seven of these infants had trisomy 21. Fortunately, only two pregnancies were terminated for soft findings. In both cases, this action had not been advised by the prenatal diagnosis team and, in both cases, the fetus was normal at autopsy.

The investigation confirms the value of routine ultrasound in the identification of serious anomalies, but it raises questions about the expanding use of soft ultrasound markers in such screening programs. ❖

Which of the following anomalies is most likely to be detected on routine ultrasound examination?

a. Ultrasound
b. Cleft lip
c. Diaphragmatic hernia
d. Ventricular septal defect
e. Spina bifida

Effect of Alendronate on Risk of Fracture in Women With Low Bone Density but Without Vertebral Fractures

ABSTRACT & COMMENTARY

Synopsis: *Alendronate decreases the risk of fractures only in women with low bone mass or those who already have a fracture.*

Source: Cummings SR, et al. *JAMA* 1998;280: 2077-2082.

A previous study showed that alendronate use for three years reduced the risk of hip and wrist fractures by about 50% in women who had low bone mineral density (BMD) and vertebral fractures. This follow-up study tested the hypothesis that alendronate would also reduce the risk of clinical fractures in postmenopausal women who have low BMD but not vertebral fractures. A total of 4432 postmenopausal women not taking hormone replacement therapy (HRT) with low femoral neck BMD (lower than or equal to 0.68 g/cm^3) were randomized to placebo or alendronate for four years. The dose of alendronate was 5 mg daily for the first two years and 10 mg daily for the last two years. BMD was measured at the hip, spine, and whole body using a Hologic densitometer (dual energy x-ray absorptiometry [DEXA]). A subset had wrist BMD assessed. The hip and spine assessments were anually repeated. Vertebral fractures were assessed by clinical criteria and by radiographic morphometry. A decrease of 20% or 4 mm in vertebral height was classified as a compression fracture.

Compared with the placebo, alendronate use resulted in a similar increase in BMD in all women, regardless of initial BMD. However, alendronate use decreased the overall fracture rate only in women with femoral neck BMD less than -2.5 standard deviations below normal young adult mean based on results obtained by the Third National Health and Nutritional Examination Survey (T-score). The overall relative

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hazard was 0.64 for women with a T-score of less than or equal to -2.5 but 1.03 for those with a T-score higher than -2.5 and lower than -2.0. The risk of vertebral fracture detected radiographically was also reduced in women with an initial T-score less than or equal to -2.5. The relative hazard for vertebral compression fracture was 0.50 in this group, but 0.54 (confidence interval, 0.28-1.04) for those with a T-score higher than -2.5 and lower than -.0 and 0.82 or a T-score greater than or equal to -2.0 (CI, 0.33-2.07).

COMMENT BY SARAH L. BERGA, MD

This study is interesting for many reasons. First, it suggests that alendronate should not be used universally as prophylaxis against future fractures. Second, the study enrolled only women not using HRT, so at least two important questions remain unanswered. One is whether the concomitant use of HRT and alendronate makes sense for any group of postmenopausal women. The other question is whether HRT or alendronate is better for the prevention of fractures in postmenopausal women with osteoporosis. Third, the study found that an astonishing 82% of women had dietary calcium intakes of less than 1000 mg/d.

In his accompanying editorial (*JAMA* 1998;280:2119-2120), Robert Heaney, MD, highlights another interesting feature of the study, that osteoporosis is defined as skeletal fragility due to low bone mass, microarchitectural deterioration, or both. However, the practical definition of osteoporosis is based only on BMD as radiographically assessed. Not all women with low BMD have architectural fragility. The best indication of fragility is a clinically evident fracture. The prior study of women with a history of vertebral fractures assessed the effects of alendronate in women with osteoporosis due to low bone mass and fragility. But not all women with low BMD also have fragility, so, in this study, those without fragility may have benefited less and also diluted the treatment effect of alendronate. Heaney points out that there currently is no biochemical test for fragility. Personal and family histories are the best clues. He suggests that the reasonable clinician will implement bisphosphonate therapy in those with low BMD (T-score less than or equal to -2.5) and a clinical history of bone fragility or glucocorticoid use. To prevent loss of bone mass in others, he suggests HRT, exercise, and appropriate dietary calcium and vitamin D intake. Given that 82% of enrollees had inadequate dietary intakes of calcium, the prudent clinician should do what it takes to make sure that all patients get the message to get enough dietary calcium and vitamin D. Since HRT has benefits above and beyond the prevention of fractures, its use should be strongly encouraged. Like nutritional intake, HRT use is woefully low. We should concentrate on understanding why and figuring out what it will take to make HRT more acceptable and tolerable to a larger group of women. It is unsatisfying to wait for fracture to occur before starting an intervention, because, by that time, the loss of microarchitectural integrity can never be fully reversed. To Heaney, that is a lot like waiting for a stroke before treating hypertension. However, the present data do not suggest that alendronate should be given as the first line of defense for prophylaxis from osteoporosis. ❖

Which of the following statements is true?

a. Alendronate use increases bone mass but does not decrease fracture rates in all women.
b. Most women get enough calcium in their diets, but they do not get enough vitamin D.
c. HRT is far better than alendronate for the prevention of fractures.
d. Alendronate is far better than HRT for the prevention of fractures.
e. It is dangerous to give HRT and alendronate together.

Tamoxifen and Ocular Toxicity

ABSTRACT & COMMENTARY

Synopsis: *A cross-sectional study of women taking tamoxifen found no evidence of vision-threatening ocular toxicity.*

Source: Gorin MB, et al. *Am J Opthalmol* 1998;125: 493-501.

A group of ophthalmologists from many medical centers conducted a cross-sectional study of 303 women with breast cancer currently taking tamoxifen. Subjective information was collected regarding vision, and testing was performed for visual acuity and color vision. In addition, each participant received a full ophthalmic examination. There was no evidence of any decrease in visual function associated with tamoxifen, except for an increased color confusion. Most importantly, there were no differences detected in corneal opacities comparing tamoxifen users with nonusers. However, the tamoxifen-treated group had greater prevalence of intrareti-

nal crystals and posterior subcapsular opacities. Gorin and associates believe this latter finding is potentially troublesome, and women receiving tamoxifen should have a baseline ophthalmic evaluation within the first year of therapy.

COMMENT BY LEON SPEROFF, MD

In the American Tamoxifen Prevention Trial, there was a statistically significant 1.6-fold increase in cataracts.[1] For this reason, I was pleased to see a well done major effort reported by ophthalmologists. Opacity changes in the eye that are drug-related are a very serious concern since they are not reversible. I find this report to be somewhat, but not wholly, reassuring.

The findings with color confusion may not be a problem. Color confusion is important because disturbances in color perception are recognized as early indications of optical dysfunction associated with diabetes, maculopathy, and optic nerve problems. When patients with these conditions were excluded, the significance was reduced.

Although no definite evidence of an increase in opacities was detected, the prevalence of posterior subcapsular opacities could be a prelude to cataract formation. Therefore, Gorin et al ended their generally negative report with a cautionary warning. They advised ophthalmologic evaluation of patients using tamoxifen.

The American Tamoxifen Prevention Trial was unblinded because there were 49% fewer cases of invasive breast cancer and 50% fewer cases of noninvasive breast cancer in the tamoxifen-treated arm of the study. These results lead me to recommend tamoxifen prophylaxis (20 mg daily for 5 years) for those women who are diagnosed with ductal carcinoma-in-situ of the breast or who have atypical hyperplasia in a breast biopsy (especially if a positive family history of breast cancer is also present). For others who seek tamoxifen preventive treatment, because of the side effects of endometrial cancer, venous thrombosis, and possible cataracts (and a basic reluctance to base clinical practice on the outcome of one study), I advise that the final answers are not in, and that clinical trial results from long-term follow-up will be necessary before fully informed decision making is possible.

Because of the gynecologic problems associated with tamoxifen, I recommend the following program for monitoring women during long-term tamoxifen treatment:

All women: Careful pelvic examination every six months to detect the emergence of endometriosis, ovarian cysts, and uterine leiomyomata.

Postmenopausal women: Annual measurement of endometrial thickness by transvaginal ultrasonography. Endometrial biopsy of all women with a two-layer thickness of 5 mm or greater. Saline instillation (sonohysterography) when appearance is not totally benign.

Premenopausal women: Periodic assessment for ovulation; if ovulatory, no further intervention is necessary; however, contraceptive counseling should not be ignored.

If anovulatory, an annual endometrial aspiration biopsy; interpretation of endometrial thickness measurements by ultrasonography is uncertain in premenopausal women. ❖

Reference

1. Fischer B, Constantino JP, Wikerham DL, et al. *J Natl Cancer Inst* 1998;90:1371-1388.

The following statements are true of long-term therapy with tamoxifen *except*:

a. Potential side effects associated with tamoxifen include endometrical cancer, cataract formation, and venous thrombosis.
b. The benefit of prevention of breast cancer outweighs the side effect problems for all women who take tamoxifen—women at both high risk and low risk for breast cancer.
c. The recommended prophylaxis regimen for tamoxifen is 20 mg daily for five years.
d. It is still unknown whether tamoxifen can reduce breast cancer mortality in women at risk for breast cancer but disease free.

Missed Opportunities for Cervical Cancer Screening of HMO Members Developing ICC

ABSTRACT & COMMENTARY

Synopsis: *Many women who develop invasive cervical cancer have not had Pap smears at the time of their routine primary care visits.*

Source: Kinney W, et al. *Gynocol Oncol* 1998;71: 428-430.

The purpose of this article was to determine whether there were opportunities for Pap smear screening at the time of routine preventive health care visits that were missed in women who later developed

invasive cervical cancer (ICC). Kinney and associates reviewed the medical records of all 642 members of the Permanente Health Plan in northern California to determine who had been seen in one of their facilities in the three years prior to the development of ICC during the years 1988-1994. Kinney et al examined the time period beginning 36 months prior to the diagnosis to six months prior to the diagnosis. The interval from six months to diagnosis was not examined in order to eliminate Pap smears that were part of the workup of the disease.

The cohorts comprised 8,498,000 woman-years of follow-up in the 642 cases of invasive cervical cancer between 1988 and 1994. Sixty percent of the women had not had a Pap smear during the study time. Of those women who met the membership criteria, 75% had outpatient visits to internal medicine, family practice, obstetrics and gynecology, or urgent care. Indeed, during the study period, the average number of clinic visits was slightly greater than five. Seventy percent of the women attending the internal medicine or family practice clinics had not had a Pap smear during the study interval, compared to 7% of the women seen by obstetrics and gynecology physicians and 20% of the women seen by urgent care physicians.

In the discussion section of the paper, Kinney et al review the fact that many efforts nationally are aimed at improving screening rates by attempting to encourage women who have not been seen for a Pap smear to do so. Much less effort has been expended trying to be certain that women who are seen in a health system for any reason have Pap smear screening at regular intervals. Kinney et al believe that their study suggests a need for increased efforts to improve screening among women who attend a medical facility.

COMMENT BY KENNETH NOLLER, MD

Despite a few limitations, this is an excellent article. The subject matter is good, the design is clear, the results are understandable and meaningful, and the writing is succinct (2 pages) and crisp. The one major limitation of the study was pointed out by Kinney et al: Some women would have had a screening in the six months prior to diagnosis, and, thus, the percentages quoted in the article are almost certainly somewhat low. Kinney et al are performing additional studies to examine this time interval.

I doubt very much whether anyone is reading this unless he or she is a dedicated advocate of women's health. Whether we call ourselves an obstetrician/gynecologist, family physician, internist, nurse clinician, or some other name, we must be advocates among our colleagues for Pap smear screening. There is simply no justification for a woman to be seen repeatedly year after year and not have cervical cancer screening. The Pap smear is, by far, the best cancer screening tool ever developed. Mammography is good but pales in comparison to Pap smear screening. Indeed, we could nearly wipe out cervical cancer if every woman had a Pap smear at regular intervals. This year alone, 15,000-20,000 new cases of invasive cancer of the cervix will occur in the United States. ❖

Among women developing invasive cervical cancer, Kinney et al discovered that the highest rate of Pap smear screening was performed in which of the following clinicals

a. Internal medecine
b. Family practice
c. Obstetrics & gynecology
d. Urgent care

Relationship Between HPV Type 16 in the Cervix and Intraepithelial Neoplasia

ABSTRACT & COMMENTARY

Synopsis: *Women with persistent Human Papillomavirus Type 16 infection are more likely to develop cervical intraepithelial neoplasia than those with transient infection.*

Source: ter Harmsel B, et al. *Obstet Gynecol* 1999; 93:46-50.

In their introduction, ter hamsel and associates point out that the data that have previously been published concerning the development of cervical intaepithelial neoplasia and the presence of Human Papilomavirus Type 16 (HPV Type 16) viral infection are "not straightforward." Although a large number of women are known to be infected with the virus, few HPV 16-infected women ever develop neoplasia. The purpose of this study was to determine whether there was an association between the persistence of an HPV 16 infection and the later development of CIN.

At the hospital of ter Harmsel et al, all women who had Pap smears performed in the gynecology department during the years 1988 and 1989 also had screening for HPV 16 infection using PCR technology. Those women who had a positive screen for HPV 16 and had a normal smear were asked to return at six-month intervals for repeat testing. After three consecutive tests had

been performed, the study participants were divided into those who had three consecutive HPV 16-positive tests and those who did not.

Of the 5500 women who were screened, 110 (2%) were found to be HPV 16-positive. Thirty-two of these women had an abnormal Pap smear and were excluded. Fifty-four of the remaining 78 women consented to be part of the study. Twenty-five of these 54 had persistent infections, and 29 did not. Eleven of the twenty-five (44%) women with persistent infections developed CIN, whereas only six of the 29 (21%) women who had transient infections did so (P = 0.036). The CIN in those women with persistent infection tended to be more advanced.

In the discussion section of the paper, ter Harmsel et al suggest that women who have positive HPV 16 tests should be monitored "more closely" because of their increased risk of developing CIN. They further suggest that the routine use of HPV testing would not be cost-effective, even though they used a low estimate of the cost of each HPV test. ter Harmsel et al suggest that women with (atypical squamous cell of undetermined significance) smears might represent a sub-group for whom HPV 16 testing might be cost-effective, but their study did not address this issue.

COMMENT BY KENNETH NOLLER, MD

Considerable discussion occurs at every cytology meeting, colposcopy meeting, and constantly in the literature regarding the role of HPV testing. There is no doubt that those women who are infected with one of the high-risk virus types (and HPV 16 is by far the most common in the United States) are at higher risk for developing CIN than women who are not infected. Yet, few women who are infected with HPV 16 ever develop detectable CIN. Almost no one would argue for the routine use of HPV 16 testing of all women because it would add an enormous cost to the U.S. health care system. However, there might be a sub-group for whom such testing would be appropriate. For example, ter Harmsel et al suggest that women with ASCUS smears might represent an appropriate sub-group. Presumably, those women with ASCUS smears who were high-risk HPV type positive would continue to be frequently screened. Those who were HPV negative would stop the screenings and return to routine, once yearly Pap smear screening. Indeed, in any algorithm that uses HPV testing, those women who are HPV negative, regardless of their initial status, must be returned to annual screening for the test to be cost-effective.

The controversy will continue—probably far into the future. This current article certainly does not help us very much in our clinical practices. Rather, it is an interesting anecdote. ❖

In the article by ter Harmsel et al that describes a relationship between HPV and the development of CIN, which of the following statements is true?

a. Most women who test positive for HPV 16 develop CIN.
b. Women who test positive for HPV 16 on three consecutive smears six months apart are at high risk for the development of CIN.
c. There is no difference between transient or persistent HPV infection when considering the rate of development of CIN.
d. HPV 16 testing was shown by ter Harmsel et al to be cost effective for the evaluation of women with ASCUS smears.

Postmenopausal Hormone Therapy and Hypertension

ABSTRACT & COMMENTARY

Synopsis: *Postmenopausal hormone therapy is not contraindicated in women with hypertension.*

Source: Lloyd G, Jackson G. *J Hum Hypertens* 1998; 12:319-321.

Lloyd and jackson from the cardiothoracic Centre at Guy's and St. Thomas' Hospital in London reviewed the relationship between postmenopausal estrogen treatment and hypertension. They point out that a large number of in vivo and in vitro studies demonstrate that estrogen has multiple effects on the vascular system that are consistent with vasodilatation, not vasoconstriction. Clinical studies, such as the three year PEPI trial, have documented no significant effects of oral hormone therapy on blood pressure (either estrogen alone or estrogen combined with sequential progestational agents). In a prospective, randomized trial, transdermal estrogen administered to hypertensive women was associated with a 3 mm decrease in blood pressure.[1] Lloyd and Jackson conclude that postmenopausal hormone therapy (PHT) either has no effect on blood pressure or a mild antihypertensive effect.

COMMENT BY LEON SPEROFF, MD

Hypertension is both a risk factor for cardiovascular mortality and a common problem in older people. Therefore, it is important to realize that no relationship has been established between hypertension and the doses of estrogen used for postmenopausal therapy. Studies have either shown no effect or a small, but statis-

tically significant, decrease in blood pressure due to estrogen treatment. This has been the case in both normotensive and hypertensive women. The addition of a progestin does not affect this response. Discontinuing hormone therapy in women with hypertension does not result in a decrease in blood pressure (an expected response if the treatment were raising blood pressure), and in some patients, discontinuation is followed by an increase in blood pressure.[2] The rare cases of increased blood pressure due to oral estrogen therapy truly represent idiosyncratic reactions. Because of the protective effect of appropriate estrogen treatment on the risk of cardiovascular disease, it can be argued that a woman with controlled hypertension is in need of that specific benefit of estrogen. Indeed, in the Nurses' Health Study, hypertensive women who used postmenopausal hormone therapy did have a reduced risk of coronary heart disease.[3] Although this position has been challenged by the results of the HERS trial, the problems with the HERS (reviewed in a previous issue of Clinical Alert), combined with the large amount of evidence supporting a beneficial effect of estrogen do not support the contention that hypertension is a contraindication to postmenopausal therapy.

In view of the results of the HERS trial, is it reasonable to choose a progestational agent other than medroxyprogesterone acetate for hypertensive women? There is reason to believe that the continuous presence of medroxyprogesterone acetate could attenuate and even block the favorable effects of estrogen on atherosclerosis and vasomotor function. There is evidence in the monkey that medroxyprogesterone antagonizes the favorable effects of conjugated estrogens on both the process of atherosclerosis and vasodilatation, but progesterone did not interfere with the ability of estrogen to inhibit atherosclerosis. In a study of mechanisms involved in the regression of atheroscleorsis, conjugated estrogens did exert favorable activity (aortic connective tissue remodeling in response to lipid lowering) in the monkey, but medroxyprogesterone acetate prevented this action.[4] At this time, I believe it is prudent to choose progestational agents other than medroxyprogesterone acetate in hormonal regimens for hypertensive women. ❖

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3. Grodstein F, et al. *N Engl J Med* 1996;335:453-461.
4. Register TC, et al. *Arterioscler Thromb Vasc Biol* 1998;18:1164-1171.

The following statements are true regarding postmenopausal hormone therapy and hypertension *except*:

a. Observational studies and randomized clinical trials have not documented a hypertensive effect of postmenopausal estrogen therapy.
b. Oral estrogen therapy does not cause rare idiosyncratic increases in blood pressure.
c. Women with hypertension should not use oral hormone therapy.
d. Clinicians should consider progestin options other than medroxyprogesterone acetate in women with hypertension.

Special Feature

The Role of Prophylactic Oophorectomy in Women at High Risk of Ovarian Cancer

By David M. Gershenson, MD

Approximately 10% of all epithelial ovarian cancers are hereditary. When the BRCA1 gene was cloned in 1994, lifetime estimates of risk of ovarian cancer for women with BRCA1 germline mutations were as

high as 70-80%. Such estimates are now judged to be excessively high based on the fact that early studies were conducted using very high-risk families. Current estimates of lifetime risk of ovarian cancer associated with a BRCA1 germline mutation are approximately 30%. A mutation of the BRCA2 gene, first cloned in 1995, appears to confer a lifetime risk of ovarian cancer in the range of 10%. For women with a family history of ovarian cancer, enrollment in a comprehensive ovarian cancer screening and genetics program should be considered. In such a program, based on family pedigree analysis, women are categorized as either low-risk or high-risk for ovarian cancer. High-risk women are offered genetic testing. However, some may decline testing for myriad reasons, including concern about confidentiality. For high-risk women, with or without genetic testing, there are several alternatives available for risk reduction or screening. If a woman has completed childbearing or is beyond a certain age, prophylactic oophorectomy is an important consideration. Other alternatives include use of oral contraceptives or screening with periodic transvaginal sonography and serum CA 125 testing. Evidence from multiple epidemiologic studies indicates that oral contraceptive use may reduce a woman's risk of ovarian cancer as much as 50% if taken up to five years. Based on recent data, this protection appears to be equally effective for women with BRCA1 and BRCA2 mutations. Although there is no effective screening method for ovarian cancer for the general population, several centers are focusing on high-risk women. The efficacy of ultrasound and CA 125 testing in this population remains to be defined. There is also some evidence that retinoids may decrease risk of ovarian cancer. More study is required in this area.

For those women who elect prophylactic oophorectomy, the laparoscopic approach is favored. A separate decision is that of whether to combine the procedure with hysterectomy. Although prophylactic oophorectomy seems to be a simple, effective method of ovarian cancer prevention, the facts are not so straightforward. Some women who undergo the procedure will subsequently develop primary peritoneal cancer. This entity was first described by Swerdlow in 1959.[1] In a large study of primary peritoneal cancer from M.D. Anderson Cancer Center, we found that the incidence of this entity was approximately 1/10th that of epithelial ovarian cancer.[2] Histologically, it is indistinguishable from ovarian cancer with papillary serous features, and the treatment and prognosis are identical to that of advanced ovarian cancer.

In 1982, Tobacman and colleagues reported prophylactic oophorectomy performed in 28 women from 16 families at high risk of ovarian cancer.[3] Three (11%) of these women subsequently developed disseminated intra-abdominal malignancy, presumably primary peritoneal cancer. In a later report from the Gilda Radner Familial Ovarian Cancer Registry, Piver and colleges described 324 women from high-risk families who underwent prophylactic oophorectomy.[4] Six (1.8%) developed primary peritoneal cancer one, two, five, 13, 15, and 27 years after the operation. In a preliminary report of a multicenter study, Struewing and associates described eight ovarian cancers among 346 non-oophorectomized first-degree relatives of ovarian or breast cancer patients, compared with two cases of peritoneal carcinomatosis among 44 oophorectomized women.[5] Compared with the Connecticut Tumor Registry data adjusted for age, race, and birth cohort, there was an approximately 24-fold excess of ovarian cancer among non-oophorectomized women, and a 13-fold excess of primary peritoneal cancer among oophorectomized women. This difference was not statistically significant. Struewing et al stated that a collaborative analysis will be required to determine whether the apparent protective effect of prophylactic oophorectomy is real.

In summary, prophylactic oophorectomy is a good alternative for ovarian cancer prevention in women at high risk for the disease based on family history or genetic susceptibility testing. The true incidence of subsequent primary peritoneal cancer remains unknown, and further study will be necessary to determine it. In the meantime, women contemplating prophylactic oophorectomy should be counseled about available information on primary peritoneal cancer. Regardless of the ultimate data, risk reduction with this procedure appears to be substantial. ❖

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In Future Issues:

Luteal Phase Deficiency and Anovulation in Recreational Women

1995;17:33-35.

The risk of primary peritoneal cancer after prophylactic oophorectomy in women at high risk of ovarian cancer appears to be in the range of:

a. 2-15%.
b. 15-20%.
c. 35-40%.
d. 50%.
e. greater than 50%.