AMERICAN HEALTH CONSULTANTS® A Medical Economics Company

OB/GYN CLINICAL ALERT®

A monthly update of developments in female reproductive medicine

American Health Consultants Home Page—http://www.ahcpub.com

CME for Physicians—http://www.cmeweb.com

HRT and Risk of Breast Cancer With a Favorable Histology

TRIAL COVERAGE

The iowa women's health study is a population-based random sample of postmenopausal women who were aged 55-69 in 1986. A total of 1520 incident breast cancers have occurred in the at-risk cohort of 37,105 women. Gapstur and colleagues utilized this population sample to determine if past or current hormone replacement theory (HRT) use was a risk factor for the development of breast cancer. The survey instrument was a questionnaire, but the type of HRT used was not elicited. To make this analysis more informative, Gapstur et al asked whether the relationship between postmenopausal hormone use and breast cancer varied by tumor type. Based on standard histologic criteria, the breast cancers were put into one of four categories. Ductal carcinoma in situ (DCIS) accounted for 11.5%, 5.4% were deemed invasive breast cancer with a favorable histology, 76.6% were called infiltrating ductal or lobular carcinoma, and 7% were other. The last group was not included in the analysis. Age at menarche, age at menopause, and type of menopause were not related to the age-adjusted incidence of any tumor type. A positive association between age at first birth and breast cancer risk was seen for all histological tumor types. Family history of breast cancer increased the risk of DCIS and invasive ductal or lobular carcinoma with an unfavorable prognosis. Overall,Gapstur et al found a positive association between HRT use and-incidence of breast cancer only for those with breast cancers deemed "favorable." This subgroup accounted for only 5% of the tumors, and the risk was largely confined to current use. Interestingly, in this subset, the risk of breast cancer was less in those who used hormones more than five years than in those who used hormones postmenopausally for less than five years. Conversely, the incidence of DCIS and invasive ductal or lobular carcinoma were not related to past or current use, regardless of duration. (Gapstur SM, et al. *JAMA* 1999;281:2091-2097.)

COMMENT BY SARAH L. BERGA, MD

In seeking to determine if postmenopausal hormone use increases the risk of breast cancer, Gapstur et al sought to improve upon the

Volume 16 • Number 4 • August 1999 • Pages 25-32

INSIDE

usual and customary design by stratifying breast cancer into histologic types and then considering the effect of HRT use upon these subtypes. Otherwise, the study is a standard epidemiological trial in which a large cohort of women were observed prospectively. I have long felt that it makes little sense to lump all breast cancers together. Certainly, not all breast cancers are the same, one must consider stage, host, histology, or causal molecular and cellular derangements. The logic of subtyping is compelling, but it is not clear what criteria should be used to subtype. For instance, it has been shown that mutations in tumor suppressor genes [p53, BRCA, BRCA 2, ATM (ataxia-telangiectasia, mutated)] or overexpression of oncogenes (such as Her-2-Neu) are causally related to the development of breast cancer. Ideally, one would subtype according to relevant molecular features. Since molecular fingerprinting of breast cancers was not possible, Gapstur et al resorted to the best criteria that could bedevised in this setting. It is debatable if the subtypes represent relevant biological groups. If they do not, one can argue that the data must remain aggregated rather than segregated. If the data remain aggregated, then this is a large study showing that current and past HRT use does not increase the risk of breast cancer. If one allows that the subtyping is biologically valid, then the study suggests, as have others like it, that HRT use may promote the development of breast cancers with a favorable prognosis in a small minority of women. Put another way, cancers that develop in women "due" to HRT have a good prognosis. However, given the tentative nature of the subgroups, the most conservative conclusion to draw from this data set is that HRT use does not promote the development of breast cancer. Most breast cancers occur independently of past or current HRT use. I tell patients that we do know a little about what causes breast cancer, and it does not appear to be estrogen exposure. ❖

OB/GYN Clinical Alert, ISSN 0743-8354, is published monthly by American Health Consultants, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

VICE PRESIDENT/GROUP PUBLISHER: Donald R. Johnston.

EXECUTIVE EDITOR: Glen Harris.

MARKETING PRODUCT MANAGER: Schandale Kornegay.

ASSISTANT MANAGING EDITOR: Robin Mason.

COPY EDITORS: Holland Johnson, Neill Larmore, Michelle Moran.

Registration Number: R128870672.

Periodical postage paid at Atlanta, GA.

POSTMASTER: Send address changes to ***OB/GYN Clinical Alert***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $17. One to nine additional copies, $100 each; 10 or more additional copies, $60 each. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.

This is an educational publication designed to present scientific information and opinion to health professionals to stimulate thought and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.

Subscriber Information

Customer Service: 1-800-688-2421

Editorial E-Mail: holland.johnson@medec.com

Customer Service E-Mail: customerservice@ahcpub.com

Subscription Prices

United States

$199 per year (Student/Resident rate: $100).

Canada

$243 per year including GST

(Student/Resident rate: $110 including GST).

Elsewhere

$229 per year (Student/Resident rate: $110).

Accreditation

American Health Consultants is accredited by the Accreditation Council for Continuing Medical Education (ACCME) to sponsor CME for physicians. American Health Consultants designates this CME activity for 25 credit hours of Category 1 of the Physician's Recognition Award of the AMA. This CME activity was planned and produced in accordance with the ACCME Essentials. The program has been reviewed and is acceptable for 20 Prescribed hours by the American Academy of Family Physicians. Term of approval is for one year from beginning distribution date of 1/99 with option to request yearly renewal. **For 25 Category 1 CME credits, add $50.**

Questions & Comments

Please call **Robin Mason,** Assistant Managing Editor, at (404) 262-5517 or **Holland Johnson**, Copy Editor at (404) 262-5540 between 8:30 a.m. and 4:30 p.m. ET, Monday-Friday.

Statement of Financial Disclosure

American Health Consultants does not receive material commercial support for any of its continuing medical education publications. In order to reveal any potential bias in this publication, and in accordance with Accreditation Council for Continuing Medical Education guidelines, we disclose that Dr. Speroff is involved as a consultant, and is in research for Wyeth Ayerst, Parke-Davis, Ortho, and Novo Nordisk. Dr. Berga is a consultant for Parke-Davis, Organon, and Women First, Inc., and is involved in research for Berlex and Health Decisions, Inc. Dr. Gershenson is involved in research for Pharmacia- Upjohn, Oncotech, Genetech, SmithKline Beecham, Atairigen, and the National Cancer Institute. Dr. Morrison serves as a consultant for Zeneca. Dr Noller and Dr. Gabbe report no relationships.

Therapy for Intraductal Carcinoma of the Breast

ABSTRACT & COMMENTARY

Synopsis: *Tamoxifen added to lumpectomy and radiation therapy improves outcome after treatment of intraductal carcinoma in situ of the breast.*

Source: Fisher B, et al. *Lancet* 1999;353:1993-2000.

The national surgical adjuvant breast and Bowel Project B-24 was a double-blind, randomized, controlled trial, comparing lumpectomy, radiation therapy, and tamoxifen with lumpectomy and radiation therapy alone for ductal carcinoma in situ of the breast. A total of 1804 women with ductal carcinoma in situ participated in the study, including those whose resected sample margins were involved with a tumor. Each group involved 899 patients. The tamoxifen-treated group had an 8.2% incidence of breast cancer events at five years compared with 13.4% in the placebo group, including events in both the ipsilateral and contralateral breasts. The relative risk indicated a 37% reduction in breast-cancer events in the tamoxifen-treated group. In ipsilateral breasts, tamoxifen treatment produced a 44% reduction in invasive disease. In contralateral breasts, therewas a 52% reduction in breast tumors in the tamoxifen-treated group. Fisher and colleagues conclude that the combination of lumpectomy, radiation therapy, and tamoxifen is more effective than lumpectomy and radiation therapy alone, with the added benefit of a decrease in the rate of invasive cancer in the ipsilateral breast.

COMMENT BY LEON SPEROFF, MD

Until the mid-1980s, ductal carcinoma in situ of the

breast was treated by mastectomy and axillary dissection. Before the availability of mammography, less than 3% of newly diagnosed breast cancers were ductal carcinoma in situ. With the improvement in and greater availability of diagnostic equipment, 20-30% of mammographically-detected cancers are now ductal carcinoma in situ. The National Surgical Adjuvant Breast and Bowel Project reported in 1993, and again in 1998, that lumpectomyand radiation therapy were effective treatments, and thatmastectomy was not warranted in women who had ductal carcinoma in situ. This report demonstrates that the addition of tamoxifen (10 mg bid for 5 years) improves theoutcome with all breast cancer events, including invasive and non-invasive tumors in the ipsilateral breast, in thecontralateral breast, and at metastatic sites. After five years, lumpectomy alone is associated with a 25% incidence of breast cancer-related events. Adding radiotherapy reduced the percentage to 13%. Adding radiotherapy and tamoxifen reduces the percentage to 8%. A study is currently underway to determine the effectiveness of tamoxifen in treating ductal carcinoma in situ after lumpectomy without radiation therapy.

Because mammography has made the diagnosis of ductal carcinoma in situ of the breast relatively common, the proper management of this carcinoma in situ is a major issue. Although ductal carcinoma in situ is viewed as a precursor to invasive disease, this does not always occur. Because of the small but real chance of invasive disease, women with ductal carcinoma in situ have often been treated with mastectomy. There has not been a trial comparing the results with mastectomy to lumpectomy and radiotherapy. Cancer clinicians accept that there is a low, although not zero, rate of occurrence after mastectomy. The possibility exists that a combination of lumpectomy, radiation therapy, and tamoxifen may bring the risk of recurrence to a rate that is comparable to mastectomy. Adding tamoxifen treatment to lumpectomy and radiation therapy makes the decision to avoid mastectomy relatively easier.

These results are relevant to the use of tamoxifen for the prevention of breast cancer. In my view, the administration of tamoxifen to healthy women is not a clear-cut necessity. Added to the real incidence of side effects, including endometrial cancer, venous thrombosis, and possibly cataracts, there is also the concern that tamoxifen treatment is not preventing, but delaying the onset of breast cancer. For this reason, the decision to take tamoxifen as preventive treatment is not an easy one for healthy women. The data offers convincing evidence that women with ductal carcinoma in situ of the breast, or atypical hyperplasia in a breast biopsy, are good candidates for tamoxifen treatment. ❖

Preterm Breech Delivery: Cesarean vs. Vaginal Delivery

ABSTRACT & COMMENTARY

Synopsis: *Cesarean delivery for early preterm breech delivery at 26-31 weeks does not improve survival without disability or handicap.*

Source: Wolf H, et al. *Br J Obstet Gynaecol* 1999;106: 486-491.

To determine the best route of delivery for the early preterm fetus in a breech presentation, Wolf and colleagues performed a retrospective comparison of all singleton infants delivered between 1984-1989 at a gestational age of 26-31 weeks at two hospitals in The Netherlands, one center preferring vaginal delivery, while the other favored cesarean delivery. Infants with fetal malformations and pregnancies complicated by placenta previa, placental abruption, fetal death, or a non-reassuring fetal heart rate pattern before the onset of labor were excluded. The primary outcome measure was survival without disability or handicap at follow-up two years after delivery. Both centers administered corticosteroids to accelerate fetal lung maturity, and continuous electronic fetal heart rate monitoring was used during labor. Epidural anesthesia was never used for vaginal delivery nor were episiotomies or forceps routinely used.

There were 101 preterm breech infants delivered in the center which preferred vaginal delivery and 46 in the center which favored cesarean delivery. The cesarean delivery rate was 85% in the hospital preferring this route and 17% in the other center. Of note, in the center preferring cesarean delivery, 13% of the labors progressed too fast and a vaginal delivery was performed while in the center which favored vaginal delivery, the attending obstetrician performed a cesarean delivery in 17% of cases for non-reassuring fetal heart rate patterns, cord complications, infection, or a high presentation. To avoid bias, these infants were analyzed as if they had been delivered by the route preferred in that center. Follow-up was obtained on more than 90% of the infants.

No significant difference in survival without disability or handicap was noted between the centers. Only higher birthweight (odds ratio 2.0 for each additional 250 grams) and corticosteroids given more than 24 hours before birth (odds ratio 2.7) were found to have a significant improve-ment in outcome, while footling breech presentation had a negative influence (odds ratio 0.4). Maternal morbidity was more likely at the center preferring cesarean delivery. The length of stay was sig-

nificantly longer by 2.1 days and the instance of postpartum fever, fever greater than 38°C for more than two days, was increased from 3% to 9%.

Wolf et al conclude that cesarean delivery for early preterm breech delivery at 26-31 weeks does not improve survival without disability or handicap.

COMMENT BY STEVEN G. GABBE, MD

The preferred route of delivery for the preterm breech infant remains controversial. Those who advocate cesarean delivery point to an increased risk of head entrapment, birth asphyxia, or traumatic injury with resulting long-term morbidity as reasons for this choice. Yet, there are no prospective, randomized studies to support this position. Such trials have been attempted, but failed when physi-cians were unwilling to enter their patients in the random-ization process. As noted by Wolf et al, they would haveneeded 1000 patients in their study to achieve statistical significance. They chose a unique study design including two centers in The Netherlands responsible for approximately 20% of early preterm births in that country, each with a different approach to preterm breech delivery. And, as in other retrospective studies, they were unable to document a difference in survival without disability or handicap. Furthermore, women who had a cesarean delivery required an extension of the incision into the uterine corpus or a "T" incision in eight of 17 (47%) cesareans in the center preferring vaginal birth, and six of 39 (15%) in the hospital preferring cesarean delivery, increasing the risks for uterine rupture in a future pregnancy. Despite these findings, given the medicolegal climate and the relatively limited experience with vaginal breech delivery duringthe past two decades, it is likely that most obstetricians in the United States will continue to favor cesarean delivery for the early preterm breech infant. ❖

Low-Dose Oral and Vaginal Misoprostol for Cervical Ripening and Labor Induction

ABSTRACT & COMMENTARY

Synopsis: *A 50-mcg dose of oral misoprostol is somewhat less effective than a 25-mcg dose of intravaginal misoprostol given every four hours for cervical ripening.*

Source: Wing DA, et al. *Am J Obstet Gynecol* 1999; 180:1155-1160.

Many physicians are interested in oral misoprostol for cervical ripening and the induction of labor. Wing and colleagues from the University of Southern California randomized 220 women with medical or obstetric indications for labor induction to either 50 mcg of oral misoprostol or 25 mcg of intravaginal misoprostol every four hours. At enrollment, all subjects had a Bishop score less than 5. After 24 hours, the misoprostol was stopped. Those women with a Bishop score more than 7 began induction of labor with oxytocin. When subjects began active labor, they received routine intrapartum management, including oxytocin augmentation if needed, without regard to treatment group. The primary outcome measure was successful labor induction, defined here as vaginal delivery occurring within 24 hours after that start of induction.

Of the orally treated women, 30.9% had successful labor inductions, compared with 47.3% of vaginally treated women, a statistically significant difference ($P = 0.01$). The oral treatment group required a mean of 29.6 hours to deliver, while the vaginal treatment group required 25.4 hours ($P = 0.03$). The oral misoprostol group required a mean of 3.3 doses, the vaginal group 2.3 doses ($P < 0.0001$). Approximately 75.4% of the oral group required oxytocin, compared with 59.1% of the vaginal misoprostol group ($P = 0.01$). There were no significant differences in rates of uterine tachysystole, hyperstimulation, chorioamnionitis, neonatal outcomes, or cesarean deliveries between the two groups.

COMMENT BY ELIZABETH MORRISON, MD, MSEd

Misoprostol is an effective, safe, and inexpensive choice for cervical ripening and labor induction. Oral administration will allow outpatient cervical ripening, an attractive and cost-saving option for patients, physicians, and health systems. Recent research has focused on determining the best dose for oral misoprostol.

Oral misoprostol fans will be somewhat disappointed with the results of the study by Wing et al. For all outcome measures, low-dose oral misoprostol was significantly less effective than intravaginal misoprostol for ripening the cervix and inducing labor, although both the oral and vaginal doses appeared quite safe, and both allowed labor induction within a mean of 30 hours.

Several points should be taken into account when interpreting the results of this study. Subjects included women with varying gestational ages, less than 10% of the subjects were postdates. Women with hypertension and diabetes mellitus made up one-quarter of the study population, and their concomitant medical problems might have caused them to react differently to the misoprostol. Since the study medications were discontinued after 24 hours, it was not possible to determine whether the oral misoprostol might have had a stronger effect if

given less frequently but, as other studies are exploring, for a longer treatment period.

These caveats aside, the study by Wing et al continues to support the idea that a 50-mcg oral misoprostol dose may be less effective than one would desire for cervical ripening at or near term. The answer may ultimately lie in using a higher dose of oral misoprostol with a less frequent dosing interval. Other investigators have found that a 100-mcg dose of oral misoprostol is as safe and effective as the same dose given intravaginally.[1] Oral doses of 200 mcg have also been studied,[2] but tend to cause unacceptably high rates of uterine hyperstimulation.

It will be fascinating to see the results of ongoing and future studies of 100-mcg, 50-mcg, and even 25-mcg oral doses of misoprostol for cervical ripening. We also need to know how various oral misoprostol doses compare with placebo. When these issues are resolved, many of us hope to be able to offer appropriately-selected women the option of oral misoprostol for cervical ripening and labor induction. Although Wing et al did not find a 50-mcg dose given every four hours to be as effective as they had hoped, another dosing regimen may be found that is more effective in future studies. ❖

References

1. Toppozada MK, et al. *Int J Gynaecol Obstet* 1997;56: 135-139.
2. Adair CD, et al. *Obstet Gynecol* 1998;92:810-813.

BRCA1 Inhibition of Estrogen Receptor Signaling in Transfected Cells

ABSTRACT & COMMENTARY

Synopsis: *The protein product of the gene BRCA1 inhibited estrogen-induced signaling by blocking the ability of estrogen receptor-alpha to initiate DNA transcription. This action of BRCA1 was specific to breast and prostatic cell lines and was not seen in a cultured cervical cancer cell line.*

Source: Fan S, et al. *Science* 1999;284:1354-1356.

Mutations of the breast cancer susceptibility gene BRCA1 confer increased risk of breast, ovarian, and prostatic cancer, but it is not clear why the mutations are associated with these particular tumor types. In this study, Fan and colleagues performed transient transfection assays to assess the role of wild-type BRCA1 in immortalized cell cultures of breast, prostatic, and cervical cancer. They found that the protein product of the gene BRCA1 inhibited signaling by the ligand-activated estrogen receptor-alpha (ER) to estrogen-response elements of the DNA. BRCA1 did this by blocking the function of the transcription activator called AF-2, which is a part of the estrogen receptor-alpha. This function of wild-type BRCA1 was seen in breast and prostate cancer cell lines, but not in cervical cancer cell lines. This means that if BRCA1 is mutated, the cellular impact of estrogen upon certain cell types, such as the breast, will be enhanced due to the absence of critical molecular machinery needed to constrain DNA transcription.

COMMENT BY SARAH L. BERGA, MD

In this same issue, I review the recent *JAMA* manuscript assessing the effect of HRT upon the risk of breast cancer. In their analysis, Gapstur et al of the *JAMA* article examined the differential effect of HRT upon specific breast cancer subtypes. While subtyping makes good theoretical sense, the validity of this approach depends upon the ability to appropriately subtype the tumors. I chose this companion manuscript from *Science* to demonstrate how recent gains in understanding the molecular basis of breast cancer might lead us to more meaningful parameters by which to subtype breast cancers. Fan et al showed that wild-type BRCA1 dampens the molecular effect of estrogen upon breast cancer cells. It does this by preventing estrogen receptor-alpha from having its full effect when it binds to estrogen response elements (EREs) of the DNA. Fan et al demonstrate how BRCA1 blocks the action of AF-2, which is one of two sites within ER-alpha that initiate transcription of the DNA. In other words, BRCA1 is a "transcription blocker." Knowing this, it is easy to see how mutations of BRCA1 might permit cellular growth in cell types that contain predominantly ER-alpha to become excessive when intracellular estrogen concentrations are high enough. BRCA1 apparently only regulates the actions of ER-alpha and not the actions of ER-beta.

As Fan et al point out, ER-alpha is the major estrogen receptor of mammary epithelia, but the effect of BRCA1 or its mutations are predicted to be nil in tissues that contain primarily ER-beta, such as neural or genital tissues. It stands to reason, then, that the oncogenic potential of estrogen to cause breast cancer would be seen only in, or would be greatest in, women with abnormal cellular machinery conferred by having a BRCA1 mutation. Thus, it would be critical to confirm if estrogen promotes breast cancer specifically in women with the BRCA1 mutation. Based on the foregoing *JAMA* manuscript, it would appear that, in general, postmenopausal hormone

use does not increase the risk of breast cancer, but there may be certain subpopulations of women who would still be at risk. Obviously, it is important to be able to distinguish those at risk from those not at risk when counseling women about the long-term pros and cons of HRT.

Another interesting thought is that women with BRCA1 mutations might want to take both an estrogen and an ER-alpha-specific SERM, such as raloxifene,[1] to gain the benefits of estrogen upon the brain while blocking the actions of estrogen upon the breast. Before we can evaluate the likely pros and cons of such a strategy, however, we need to better define which tissues contain predominantly ER-alpha and which contain predominantly ER-beta. The next few years ought to be very interesting! Hopefully, this gain in knowledge about the cellular mediators of estrogen action will permit us to be able to be much more specific about who needs what "hormonal cocktail." ❖

Reference

1. Cummings SR, et al. *JAMA* 1999;281:2189-2197.

Adenocarcinoma in Situ of the Cervix: Management and Outcome

ABSTRACT & COMMENTARY

Synopsis: *Adenocarcinoma in situ of the cervix is difficult to diagnosis and manage.*

Source: Azodi M, et al. *Gynecol Oncol* 1999;73: 348-353.

Adenocarcinoma in situ of the uterine cervix is a disease that has been diagnosed since 1952. Currently the pathologic criteria for the diagnosis are relatively standardized. Unfortunately, the management of patients with this disease varies greatly from one center to another.

Azodi and colleagues performed a retrospective study at their medical center, reviewing the records of all patients who had a conization of the cervix (cold knife cone, loop excision, or laser conization) and had a diagnosis of adenocarcinoma in situ, between January 1988 and December 1996. Forty patients comprised the clinical material for this study.

The mean age of the patients with this diagnosis was 37 years. All but one patient had colposcopic evaluation prior to conization.

Seventy percent of the colposcopic biopsies showed some form of glandular cell abnormality and an additional 20% showed mixed glandular and squamous abnormalities. Twenty-five patients had a cold knife conization, eight had loop excision, and eight had laser conization. An ECC was performed after the conization specimen was obtained in 70% of the cases. Thirty percent of the ECCs that were read as negative had positive endocervical margins in the cone specimen. Many of the women had a hysterectomy as definitive treatment, and 58% of the patients with a negative ECC above the cone had residual disease in the hysterectomy specimen.

Endocervical margins were more likely to be positive with laser conization or loop excision than with cold knife conization. However, 31% of the patients with negative endocervical cone margins who underwent hysterectomy had residual cervical disease.

Eight patients had no additional therapy following the conization. All of these patients had negative endocervical and ectocervical cone margins with negative ECCs. One of these eight patients had a cytology specimen that indicated the presence of adenocarcinoma 15 months following the conization, and the hysterectomy specimen showed invasive disease.

Azodi et al drew several conclusions from this paper. First, they suggest that, at the present time, cold knife conization should be the preferred diagnostic procedure of choice in patients who have cervical glandular lesions. Secondly, ECC after cervical conization is not a reliable method to determine whether residual disease is present. Finally, though a positive endocervical cone margin is more likely to leave residual disease than a negative one, a negative endocervical margin does not guarantee that all diseased tissue has been removed.

COMMENT BY KENNETH NOLLER, MD

Several times in the last three years, I have commented on articles which reported the outcomes of series of patients with AGUS pap smears. This study goes one step further. Azodi et al identified 40 patients who had a conization procedure performed because of a glandular lesion of the cervix. Like several similar articles, they found that neither a negative ECC nor negative cone margins were good predictors of a disease-free state. At present, it appears that simple hysterectomy is the treatment of choice for patients who have adenocarcinoma in situ on a conization specimen, even if the margins are negative.

But what about the patient who wants (demands) to maintain her fertility? Certainly, if the endocervical cone margin is positive, a repeat-procedure must be performed. Once negative margins have been established, the patient needs to have frequent endocervical sampling, preferably

using an endocervical brush rather than an ECC. Based on numerous reports in the literature, I believe that there is no longer any doubt that the endocervical brush is superior to the ECC for detecting disease in the canal.

Perhaps someday we will have better indicators of residual disease, and will be able to avoid hysterectomy as the primary treatment for these women. However, in the meantime, hysterectomy must remain the treatment method of choice. ❖

Special Feature

Breaking Bad News: Balancing Honest Disclosure With Hope

By David M. Gershenson, MD

At one time or another, all obstetrician-gynecologists are in a position of communicating bad news to patients and/or their families. Such an experience may involve an obstetrical mishap, a perinatal or maternal death, a postoperative complication or mortality, care of an infertility patient, or care of a cancer patient. Most of us never received any formal training in this area. For the majority of physicians, the learning process has been derived through experience. Of course, my perspective is that of an oncologist, but the overriding principles apply in several different situations and, at one time or another, affect all practicing obstetrician-gynecologists.

Kodish and colleagues note that, in the early 1960s, the vast majority of physicians did not tell patients about a diagnosis of cancer.[1] By the late 1970s, almost all physicians believed in telling patients of a cancer diagnosis. Patient attitudes have changed dramatically as well. The medical profession is no longer held in such high esteem by many of our patients. As we near the end of this millennium, the emphasis has shifted from diagnosis to prognosis. How much do we say about the probability of remission or cure? How specific can or should we be? There are no precise guidelines, and, most importantly, the amount and nature of the disclosure should be individualized based on how much the patient wants to know at the time. As Kodish et al point out, "Doctors must be honest with their patients, but must also use common sense and understand human nature."

Breaking bad news comes easily to very few of us, even today. In general, I find that my younger colleagues are better at this process than I or my older associates. In preparing to discuss a cancer diagnosis and poor prognosis with a patient and her family, it is important to assume an attitude of caring, compassion, and sensitivity. So many of the complaints I hear about other physicians surround the stiff and insensitive manner in which they communicated bad news.

Over the past few years, several authors have addressed the issue of breaking bad news. In a nice review article, Girgis and colleagues outlined a series of 16 principles for breaking bad news.[2] Based on these principles, Girgis et al recommend several important steps: 1) ensure privacy and adequate time; 2) assess the patient's understanding; 3) provide information simply and honestly; 4) encourage patients to express feelings; 5) give a broad time frame; 6) arrange review of the situation in the immediate future; 7) discuss treatment options; 8) offer assistance to tell others; 9) provide information about support services; and 10) document information given.

Robert Buckman, a Toronto physician, has also written extensively about this subject, and has authored a wonderful book entitled, "*How to Break Bad News—A Guide for Health Care Professionals.*" Buckman recommends a six-step process that encompasses many of the same principles as those summarized by Girgis et al.[3]

His recommendations include: 1) selecting the appropriate setting and the parties to be involved (e.g., the interview should be conducted in person, not over the telephone); 2) finding out how much the patient knows; 3) finding out how much the patient wants to know; 4) sharing the information (aligning and educating); 5) responding to the patient's feelings; and 6) planning and follow-through.

Over time, each physician develops his/her own style and protocol for breaking bad news. Again, the major challenge is to balance honest disclosure with the promotion of reasonable hope for the patient. Even though I have been breaking bad news for several years, I still believe that this is a dynamic process in which one can constantly improve his/her skills. We have much to learn from our patients and about the human spirit. ❖

References

1. Kodish E, et al. *J Clin Oncol* 1995;13:1817-1822.
2. Girgis A, et al. *J Clin Oncol* 1995;13:2449-2456.
3. Buckman R. *How to Break Bad News-A Guide for Health Care Professionals.* Baltimore, MD: The Johns Hopkins University Press; 1992.

CME Questions

7. Which of the following is *not* a likely risk factor for the development of breast cancer?
- a. Mutations in the tumor suppressor gene p53
- b. Testing positive for the mutations BRCA1 and BRCA2
- c. High expression of the oncogene Her-2-Neu
- d. Estrogen use for more than five years
- e. Mother who died of breast cancer

8. The following statements are true of tamoxifen and breast cancer *except*:
- a. Tamoxifen alone is adequate adjuvant therapy after lumpectomy for ductal carcinoma in situ.
- b. The duration of tamoxifen adjuvant therapy is five years.
- c. The combination of lumpectomy, radiation therapy, and tamoxifen for ductal carcinoma in situ may be as effective as mastectomy.
- d. Twenty to 30% of breast cancers detected by mammography screening are ductal carcinoma in situ.

9. In the study by Wolf et al, which of the following significantly improved intact survival for the preterm breech infant?
- a. Cesarean delivery
- b. Complete breech extraction
- c. Forceps to the aftercoming head
- d. Corticosteroid therapy for more than 24 hours
- e. Mediolateral episiotomy

10. In the study of oral vs. vaginal misoprostol for "cervical ripening" and labor induction by Wing et al, significant differences between the oral and vaginal treatment groups were found for which one of the following outcomes?
- a Uterine hyperstimulation
- b. Neonatal Apgar scores
- c. Rates of cesarean delivery
- d Rates of labor induction within 24 hours

11. Which of the following best describes the cellular function of wild-type BRCA1?
- a. Prevents estrogens from binding to the estrogen receptor-alpha, and thereby diminishes estrogen action
- b. Mimics estrogen by binding to estrogen-response elements on the DNA and initiating transcription
- c. Causes apoptosis in breast epithelial cells only
- d. Nonspecifically promotes the cellular actions of estrogen in all cell types investigated to date
- e. Inhibits estrogen-induced signaling by estrogen receptor-alpha by blocking transcriptional activation function

12. In the article by Azodi et al, 40 patients underwent conization of the cervix for adenocarcinoma in situ. Which of the following statements regarding the conization specimen is correct?
- a. A negative endocervical margin is a good predictor of a disease-free state.
- b. A negative ECC is a good indicator of a disease-free state.
- c. There was no difference in positive cone margins between cold knife cone and loop electroexcision.
- d. Hysterectomy is the treatment of choice for adenocarcinoma in situ.

Readers Are Invited

Readers are invited to submit questions or comments on material seen in or relevant to *OB/GYN Clinical Alert.* Send your questions to: Holland Johnson—Reader Questions, *OB/GYN Clinical Alert* c/o American Health Consultants, P.O. Box 740059, Atlanta, GA 30374. Or, you can reach the editors and customer service personnel for *OB/GYN Clinical Alert* via the Internet by sending e-mail to holland.johnson@medec.com. You can also visit our home page at http://www.ahcpub.com. We look forward to hearing from you. ❖

In Future Issues:

Chaperone Use by Obstetrician/Gynecologists