CME Evaluation Inside

# CLINICAL ONCOLOGY ALERT

*A monthly update of developments in cancer treatment and research*

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## INSIDE



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*Clinical Oncology Alert*'s Editor, William Ershler, MD, is on the speaker's bureau for Wyeth and does research for Ortho Biotech. Peer reviewer V.R. Veerapalli, MD, reports no financial relationship to this field of study.

# Dietary Management of Breast Cancer-Associated Lymphedema

ABSTRACT & COMMENTARY

***By William B. Ershler, MD, Editor***

***Synopsis:*** *In a prospective clinical trial of women with lymphedema following breast cancer treatment, two dietary interventions were compared to control diet in alleviating arm swelling. There was an association of weight loss and reduced swelling. However, no significant reduction was observed in those who were placed on the low-fat diet, unless there was associated weight loss. Thus, manipulating dietary composition alone was not shown to influence lymphedema severity.*

**Source:** Shaw C, et al. Randomized controlled trial comparing a low-fat diet with a weight-reduction diet in breast cancer-related lymphedema. *Cancer.* 2007;109:1949-1956.

Despite trends toward less radical surgery for primary breast cancer, ipsilateral upper extremity lymphedema occurs in 20-40%of cases.[1] Obesity is considered a predisposing factor. In the current report three different dietary approaches were prescribed to test the hypothesis that low fat diets would reduce arm swelling, even in the absence of diet-induced weight loss. These included: (1) low total calorie (1000-1200 Kcal/day); (2) low fat (20% of total energy); and (3) control (no dietary adjustment).

A total of 64 women with breast cancer-associated lymphedema were randomized to 1 of 3 dietary programs for 24 weeks. The primary outcome measure was arm volume at 24 weeks. Results showed significant reductions in body weight ($P = 0.006$), body mass index ($P = 0.008$), and skinfold thickness, measured at 4 sites ($P = 0.044$) in the weight-reduction and low-fat groups compared with controls. However, there was no significant change in arm volume in either of the dietary groups. Nonetheless, for those who lost weight, irrespective of dietary group, there was a significant reduction in excess arm volume ($P = 0.002$).

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## COMMENTARY

Dietary interventional studies are often problematic, even when motivation is strong, such as one might imagine it would be if control of troublesome lymphedema were the desired outcome. Dr. Shaw and colleagues, hopeful to demonstrate adjustment in dietary content (ie, low fat) rather than a simple low-calorie weight loss diet would produce the desired effect. What they found, however, was that in order to demonstrate this, the study would have to include approximately 10 times the number of subjects. Those who were assigned to the low calorie diet lost weight, but not as much as expected on the basis of the prescribed diet. Those on the low fat diet were advised to supplement their caloric intake with carbohydrate and protein and were not expected to lose weight, but they did. In sum, although there were interesting trends, no conclusions about dietary composition and relief of lymphedema can be drawn from the current research.

That stated, it is gratifying to see that examining the data just on the basis of weight lost, irrespective of assigned treatment (control, low calorie or low fat) demonstrated a fairly robust correlation of weight loss and reduction in lymphedema. Not a novel finding (refs), but reassuring nonetheless.

In these days where breast conserving surgical approaches are becoming more common and deep axillary lymph node dissections less, it is likely that mastectomy associated lymphedema will be found to be less prevalent. Certainly, to repeat this trial in an appropriately powered study, a sample size of approximately 500 patients would be required, unlikely without a large scale, multi-site undertaking. For a problem that is diminishing in prevalence and an intervention that is so difficult to regulate, the limited resources available for clinical research are likely to be redirected. This provides little consequence for those with this aggravating complication of breast cancer therapy. For them, perhaps the most prudent recommendation would be to make efforts to achieve ideal body weight by a combination of diet and exercise. For those already close to ideal body weight, manipulation of dietary intake by reducing fat intake might be of some benefit, but this, of course, remains unproven. ■

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# More on Imatinib for ALL in the Elderly

ABSTRACT & COMMENTARY

***By William B. Ershler, MD, Editor***


***Synopsis:*** *Treatment of acute lymphoblastic leukemia in elderly patients remains problematic. Recent data suggests imatinib with chemotherapy is both effective and well-tolerated in elderly patients with Philadelphia chromosome-positive ALL. In the current Italian trial, imatinib and prednisone, but without additional chemotherapy, used as initial therapy, produced complete hematological remission in all 29 elderly patients treated. Treatment was oral, conducted as an out patient and well tolerated.*


**Source:** Vignetti M, et al. Imatinib plus steroids induces complete remissions and prolonged survival in elderly Philadelphia chromosome-positive patients with acute lymphoblastic leukemia without additional chemotherapy: results of the Gruppo Italiano Malattie Ematologiche dell 'Adulto (GIMEMA) LA 0201-B protocol. *Blood.* 2007;109:3676-3678.

Approximately 1/3 of adult acute lymphoblastic leukemia is Philadelphia chromosome positive[1,2] and this percentage may be even higher in the elderly[3] in

whom it is considered a negative prognostic factor.[4] Recently, a consortium of French and Belgian investigators reported the value of imatinib used with additional chemotherapy in elderly ALL patients as consolidation therapy. In that trial, at the end of one year, relapse-free survival was 58%, which compared favorably with 11% of the historic controls treated similarly but without added imatinib.[5] The current report from the Gruppo Italiano Malattie Ematologiche dell 'Adulto (GIMEMA) details their experience with imatinib as initial therapy with prednisone but without additional chemotherapy.

Thirty older adult patients (> 60 years) with Ph+ ALL received prednisone (starting at 10 mg/m2 but increased to 40 mg/m2 for at least 45 days) and imatinib 800 mg/daily. The imatinib was started after one week of prednisone alone. Twenty-nine patients were evaluable for response and all of them obtained a hematological complete remission. No major toxicity was observed and for most, treatment was conducted out patient. During the 45 day induction period, only 7 patients (23%) experienced either a dose reduction or a temporary discontinuation of imatinib due to extrahematologic toxicities. Median survival from diagnosis was 20 months (95% confidence interval [CI]: 12-not reached) and the median duration of hematological remission was 8 months (95% CI: 4-27 months). Of the 29 patients, 14 relapsed after a median time of 4 months (range, 3-28 months), 2 patients died in CR at 5 and 15 months, and 13 patients remained alive in continuous remission after a median time of 10 months from response (range 1-32 months). The probability of overall survival and disease free survival at 12 months was 74% (95%CI: 54-94%) and 48% (95% CI: 28-69%).

**COMMENTARY**

ALL, and in particular Ph+ ALL occurring in older adults has remained a challenge, primarily because the intensive cytotoxic chemotherapy regimens required to induce remission is fraught with toxicity in this age group. However, recent studies have indicated that imatinib when used with steroid and chemotherapy as either consolidation[5] or initial induction therapy[6] improves outcomes and with minimal added toxicity. The current report takes this one step further. Imatinib used with prednisone but without additional chemotherapy was shown to induce remissions and result in survival figures comparable, if not superior to conventional chemotherapy, and with manageable toxicity. Furthermore, the great majority of management was out patient, considered a definite advantage in this setting.

Thus, for newly diagnosed Ph+ ALL in older adults, imatinib alone offers an effective and well tolerated treatment choice. However, although remissions were common, they were of relatively short duration for approximately 50%. Further research may identify additional well tolerated agents (eg, vincristine) which when added, either as consolidation or during induction therapy, could improve overall remission duration and survival.

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# Parenthood after Hodgkin's Disease Treatment

ABSTRACT & COMMENTARY

***By William B. Ershler, MD, Editor***


***Synopsis:*** *There is now a growing literature describing various medical issues in long term survivors of Hodgkin's disease. One of these is infertility. In the current report, an analysis of success of achieving parenthood after treatment in a cohort of female and male patients treated between 1971 and 1998. Approximately 50% attempted pregnancy and between 60% (males) and 75% (females) were successful. Those who received radiation alone or low gonadotoxic chemotherapy were most successful.*


**Source:** Kiserud CE, et al. Post-treatment parenthood in Hodgkin's lymphoma survivors. *Br J Cancer.* 2007;96:1442-1449.

Attempted and achieved post-treatment parenthood remain issues of concern for many

survivors of Hodgkin's disease. Kiserud and colleagues from the University of Oslo examined this question in a large series of patients who were registered in a national lymphoma registry between the years 1971 and 1998. In the study, investigators addressed the success of achieving post-treatment parenthood by twice (in 2002 and 2005) surveying those female patients younger than 50 years and male patients younger than 65 years regarding the issue of post treatment parenthood. Of the 1557 Hodgkin's lymphoma patients who were registered in that database during the period, 602 were eligible for the present study and were contacted by mail. Seventy-five percent responded to the surveys. Of all the responders, 86% were younger than 40 years at the time of diagnosis. The median observation time from the last treatment to the survey was 15 years (range 3 to 34 years) with 62% of the patients diagnosed before 1989. Of those treated before 1989, 61% had received both radiotherapy and chemotherapy. For the whole group, 46% had at least one child at the time of diagnosis of Hodgkin's disease.

Of the females, 50% of females and 45% of males had attempted post treatment parenthood. All of these patients were under the age of 40 years at the time of diagnosis. By both univariate and multivariate analysis, low age and prior childlessness at diagnosis were the only variables associated with post treatment attempts at parenting. Of these, 68 females (75%) and 76 males (63%) who had attempted post treatment parenthood were successful without the use of assisted reproduction techniques. The 10-year probability of post treatment parenthood was 59% in females and 56% in males. In patients who were childless at the time of diagnosis, the 10-year probabilities of post treatment parenthood were 58% in females and 54% in males. Females aged below 30 years at diagnosis were significantly more likely to achieve post treatment parenthood compared to older females.

In both males and females, achievement of post treatment parenthood was associated with the treatment modality and dose. The type and intensity of chemotherapy was most important in this regard. Individuals (males and females) who received radiation alone or low gonadotoxic chemotherapy were most likely to conceive in the 10 years following treatment whereas those who received high gonadotoxic chemotherapy such as MOPP or high dose cyclophosphamide were less likely. Cryopreserved sperm was used for fertilization by 13 males and this was successful in ten.

## COMMENTARY

Although fertility has long been an issue for those cured of Hodgkin's disease, this study is the first to investigate long-term post treatment success at achieving parenthood in a large series of consecutive Hodgkin's disease survivors. About 47% of those in the study had attempted post treatment parenthood. Young age and childlessness at the time of diagnosis were factors associated with attempting to parent. Of those who made the attempt, 68% became parents spontaneously and another 10 (males) became fathers with the use of pretreatment cryopreserved semen. Multivariate analysis confirmed the long-held notion that type of treatment is significantly associated with success, and this, for both genders. Patients who had received radiotherapy alone or low gonadotoxic chemotherapy enjoyed the greatest success.

This report adds significantly to our understanding, primarily based upon the careful methodology employed, the large data base and the choice of the highly relevant primary outcome: the first post treatment childbirth. Prior studies had relied on semen analysis in men and the development of amenorrhea in women as predictors of infertility. Nonetheless, the current study may overestimate the actual success of achieving parenthood. For one thing, patients were excluded from analysis if they relapsed, even if there had been a significant remission duration. It is unclear whether this group had attempted parenthood and whether they were successful. Furthermore, it was not clear to what extent individuals attempted to achieve parenthood. Certainly, a number of psychological factors might come to play in responding to questionnaires on an issue such as this. Nonetheless, it is gratifying to see the relatively high rate of achieved pregnancy in these long-term survivors of Hodgkin's disease.

Although it appears the optimal success was observed in those receiving radiation alone, it was not strikingly different from those receiving low gonadotoxic chemotherapy such as ABVD. In light of the risk of long-term complications from radiation in excess of that of ABVD, issues regarding parenthood might be considered minor. Finally, females aged above 30 years at the time of diagnosis are at particularly high risk of becoming infertile. They constitute a subgroup for which cryopreservation of ovarian tissue should be considered. Males, on the other hand, have the opportunity for pretreatment cryopreservation of semen and as spermatogenesis recovers in the great majority, their potential infertility after treatment is a problem of less magnitude.

# First Cycle CA-125 Response Predicts Favorable Outcome for Ovarian Cancer Patients

ABSTRACT & COMMENTARY

***By William B. Ershler, MD, Editor***

***Synopsis:*** *In a large series of ovarian cancer patients treated with chemotherapy after primary laparotomy, the fall in CA-125 during the first and second cycles was shown to provide significant prognostic value. This simple determination may prove useful in selecting patients to receive more intensive or prolonged maintenance chemotherapy after the initial induction courses are completed.*

**Source:** Riedinger JM, et al. Change in CA 125 levels after the first cycle of induction chemotherapy is an independent predictor of epithelial ovarian tumor outcome. *Ann Oncol.* 2007;18:881-885.

Measurement of serum CA-125 has proven to be a useful indicator of prognosis for patients with ovarian cancer. Riedinger and colleagues in France conducted a mulitcenter retrospective analysis to assess the prognostic value of the CA-125 change after the first and second courses of induction chemotherapy. At the participating eight cancer centers there were 494 eligible stage (International Federation of Gynecology and Obstetrics [FIGO]) IIc-IV epithelial ovarian cancers treated between 1988 to 1996, and their clinical course was followed to the study end in May, 2005. All patients had a primary laparotomy followed by a minimum of six cycles of chemotherapy (cyclophosphamide and platinum; no patients in this series received taxane). CA -125 was measured before the first cycle of chemotherapy (baseline) and prior to each subsequent cycle.

At the time of primary laparotomy, 142 patients (28.7%) had no apparent residual disease, 123 (24.9%) had a residual disease of ≤ 1 cm in the largest diameter, and 229 (46.4%) had a residual disease >1cm. After six cycles of chemotherapy, a second look laparotomy was carried out in 194 stage III patients who were considered to be in clinical complete remission (cCR). Of these, 111 (57.2%) showed a pathological CR (pCR) while 83 (42.8%) showed incomplete response.

During the first cycle of chemotherapy the median change in CA-125 was a 65% decrease, but with a wide range (82% increase to 99% decrease). Similarly in the second cycle the median was a 61% decrease in CA-125 (133% increase to 98% decrease). The total change from baseline through the first two cycles was an 86% decrease (115% increase to 100% decrease).

The CA-125 level before the 3rd cycle of chemotherapy was found to bear a prognostic value for overall survival (OS): median OS was 1.9 years (1.6-2.1 years) for patients with a CA-125 > 35kU/L and 4.9 years (4.0-5.4 years) for patients with a CA-125 ≤ 35kU/L (hazard ratio [HR] = 2.7 (2.2-33.3; $P < 0.0001$). By univariate analysis, the changes in CA-125 during the first, second, and the sum of first and second cycles, and the absolute CA-125 level before the third cycle each had strong prognostic value for OS (all with $P < 0.0001$). In multivariate analysis, the change in CA-125 level during the first chemotherapy course ($P < 0.0001$), the absence of residual tumor mass ($P < 0.003$), and the CA-125 level before the second course ($P = 0.037$) were found to be independent prognostic variables. Furthermore, among the 194 stage III patients who underwent second look laparotomy, the frequency of pCR was 77.2% (61 of 79) in the subgroup defined by those who had a >50% reduction in CA-125 during the first cycle and a return to the normal range during the second cycle of chemotherapy. Thus, the initial change in CA-125 level after the first and second cycles of chemotherapy define a subgroup of patients with more favorable prognosis.

## COMMENTARY

Serum CA-125 level has become a very useful clinical tool for those treating ovarian cancer.[1,2] Just a few months ago in these pages we reviewed a retrospective analysis of maintenance chemotherapy conducted by the Southwest Oncology Group (SWOG) and the Gynecologic Oncology Group (GOG), in which the baseline CA-125 level just prior to the initiation of maintenance chemotherapy was found to strongly predict the risk of recurrence. Those with CA-125 levels ≤ 10u/mL were found to have a superior progression free survival (PFS) compared with higher CA-125 levels within the normal range.[3] The current report adds yet another twist. The rapidity and magnitude of the CA-125 response to the first and second cycles of chemotherapy can be used to define subgroups with varying chances of achieving pCR and prolonged overall survival. This may prove particularly useful as cooperative groups are now exploring prolonged maintenance therapy for some patients considered at higher

risk for recurrence. Factors such as the rate of decline in CA -125 during the first two cycles of initial chemotherapy and the absolute level just prior to the initiation of maintenance therapy may be useful in distinguishing those who should receive more intensive and prolonged maintenance treatment and those who might do well with lesser treatment.

One small caveat with regard to the current report is worth mentioning. Taxanes were not part of the treatment regimen at the time the data was recorded and it is possible that this active drug, now used in front line treatment for ovarian cancer, could have a different effect on CA-125 kinetics. This bears attention, and hopefully this French group, or other experts in CA-125 kinetics, will provide similar data using the more current chemotherapy combinations. ■

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# Minimizing Surgery for Young Breast Cancer Patients: Is It Safe?

ABSTRACT & COMMENTARY

***By William B. Ershler, MD, Editor***


***Synopsis:*** *The risk of local recurrence in young patients who underwent breast conserving therapy for early stage breast cancer was approximately 20% by 10 years. The risk was significantly reduced by the use of adjuvant systemic therapy.*


**Source:** van der Leest M, et al. The safety of breast-conserving therapy in patients with breast cancer aged < 40 years. *Cancer.* 2007;109:1957-1964.

Over the past several decades breast-conserving surgery has become a standard approach, primarily because survival rates are demonstrably equivalent to modified mastectomy in patients with early stage breast cancer.[1,2] However, local recurrence rates may be higher, particularly in younger women who more frequently have primary tumors with negative prognostic features. Thus, in two studies that compared the risk of local recurrence after breast-conserving surgery in younger patients and older patients, there was a nine times greater risk observed in one[3] and a five times greater risk observed in the second.[4] These have raised concern about the this procedure as standard therapy in young patients, particularly in those with other known risks.

The current retrospective analysis from the Netherlands was designed to address those prognostic factors that would indicate higher risk of local recurrence in young women with early stage breast cancer. Using a data from the Eindhoven Cancer Registry and from the practice of two large radiotherapy departments in Southern Netherlands over a 14-year period (1988-2002) there were 1554 patients who were younger than 40 years at the time of breast cancer surgery. Of these, 774 underwent breast-conserving surgery and the great majority of these (96.5%) received postoperative radiotherapy. Seven hundred fifty-eight patients were evaluable for this analysis (ie, stage I or II breast cancer) and the median duration of follow-up was 8.5 years (range, 0.9 to 16.9 years). Study endpoints were local recurrence, regional recurrence, distant recurrence, contralateral breast cancer, or death.

Of the 758 evaluable patients, chemotherapy was administered to 218 (29%) and hormone therapy was administered to 25 (3%) and 86 patients (11%) received both. Early during the 14-year period of study, it was less common to prescribe chemotherapy for lymph node negative breast cancer, but this trend changed during the study interval. For example, from 1988 to 1992, 4% of lymph node negative patients received chemotherapy compared to 10% during the years 1993 to 1997, and 48% during the years 1998 through 2002. Patients with positive lymph nodes during these intervals received chemotherapy at a proportion of 71%, 96%, and 99% respectively.

Local recurrence was diagnosed in 95 patients without evidence for distant metastatic disease. Approximately one-half of these were detected by the physician upon routine clinical evaluation and the other half by the patient herself. Curiously, by multivariate Cox regression analysis, it appears that lymph node status was not an independent prognostic factor for local recurrence.

During the interval study, 22 of the 758 patients developed regional recurrence and 209 developed distant metastasis. Fifty-nine patients developed contralateral breast cancer and 174 patients have died. Thus, the 10-year actuarial rates of these end points were 3.5% (95% CI, 1.8-5.2%), 30.4% (95% CI, 26.6-34.2%), 9.6% (95% CI, 6.8-12.4%), and 26.9% (95% CI, 23.1-30.7%), respectively. The 10-year disease free survival (ie, survival without local, regional, or distant recurrence, and without contralateral breast cancer was 55.8%). In multivariate analysis, the significantly lower risk of contralateral breast cancer was identified in patients receiving adjuvant systemic treatment (hazard ratio = 0.46: 95% CI, 0.2-0.87).

## COMMENTARY

The five- and 10-year actuarial local recurrence rates were 9% and 17.9% respectively in this series. Patients who received adjuvant systemic therapy had their risk reduced by more than 50%. These local recurrence rates for younger patients were lower than reported elsewhere (typically greater than 20% at 10 years[3-7]). However, these are difficult comparisons because of the variables in duration of study and local treatment trends, including the variable use of adjuvant chemotherapy.

It is notable that of the local recurrences observed in this study, the large majority occurred at, or near the site of the primary tumor, and only 7% developed elsewhere in the breast. This supports the notion that, at least in young women, local recurrences are not new primary tumors but more likely an indication of incompleted resected residual disease. These findings support the current practice of delivering a radiation "boost" to the local tumor bed upon completion of the standard radiotherapy course. Such has been demonstrated to reduce local recurrence rate in other studies including one conducted by the EORTC.[8]

In summary, the retrospective analysis of a fairly large series of young women with early-stage breast cancer suggest that the local recurrence rates are substantial, but can be significantly reduced by adjuvant chemotherapy and radiotherapy. The impact of a radiation "boost" to the tumor bed is also likely to be effective in reducing this untoward outcome.

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# CME Questions

**22. With regard to dietary intervention to manage breast cancer associated lymphedema, which of the following dietary interventions was shown to be most effective?**

a. Low energy (ie, low caloric intake)
b. low fat (not to exceed 20% of total food intake)
c. control (no change in dietary intake)
d. none of the above.

**23. In the Italian trail of imatinib treatment of elderly patients with Ph+ ALL, complete hematological remission was achieved in:**

a. 15%
b. 40%
c. 85%
d. 100%

**24. For male survivors of Hodgkin's disease, the likelihood of ultimately achieving success in achieving parenthood is approximately:**
a. 15%
b. 45%
c. 75%
d. 95%

**25. A decline by 50% in CA-125 level in the first cycle of chemotherapy and a return to the normal range (< 35kU/L) prior to the third cycle in the treatment of ovarian cancer is associated with:**
a. a greater chance of pCR.
b. longer disease free survival.
c. longer overall survival.
d. all of the above.
e. none of the above.

**26. Local recurrence at ten years in young women ( < 40 years) with early breast cancer treated by breast conserving surgery occurs approximately:**
a. 3% of cases
b. 20% of cases
c. 30% of cases
d. 50% of cases.

**Answers:** 22 (d); 23 (d); 24 (b); 25 (d); 26 (b)

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## Risk With Preventative Antibiotics Outweighs Benefit for Most

Sweeping new changes have been made to the guidelines for prevention of endocarditis in patients undergoing dental procedures. The new recommendations dramatically reduce the indications for dental prophylaxis and reduce the number of patients who need preprocedure antibiotics. The guideline was issued by the American Heart Association in conjunction with the American Dental Association, Infectious Diseases Society of America, and the Pediatric Infectious Diseases Society and was published online April 19, 2007, in *Circulation*. The guidelines reflect evidence that the risk of taking preventative antibiotics outweighs the benefit for most patients. It is also been found that infectious endocarditis (IE) is more likely to result from frequent exposure to random bacteremias from activity such as flossing and brushing than from dental work. Specifically, the guidelines say that prophylactic antibiotics are no longer required for patients with mitral valve prolapse, rheumatic heart disease, bicuspid valve disease, calcified aortic stenosis, or congenital heart conditions such as ventricular septal defect, atrial septal defect, and hypertrophic cardiomyopathy. There are still patients who are at extremely high risk of IE who should continue to receive prophylactic antibiotics: patients with artificial heart valves, a history of infective endocarditis, congenital heart disease including unrepaired or incompletely repaired cyanotic congenital heart disease, including those with palliative shunts and conduits, those with a completely repaired congenital heart defect with prosthetic material during the first 6 months after the procedure, repaired congenital heart defect with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device, or a cardiac transplant patient with a cardiac valvulopathy. Antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease. Dosing regimens are essentially the same as previous recommendations and include oral amoxicillin 2 gm 30 to 60 minutes prior to procedure. Oral alternatives include cephalexin, clindamycin, azithromycin or clarithromycin. Parenteral regimens include ampicillin, cefazolin, ceftriaxone, and clindamycin. The guideline also no longer recommends antibiotics to prevent IE in patients undergoing genitourinary or gastrointestinal tract procedures (*Circulation* 2007, doi:10.1161/CIRCULATIONAHA.106.183095). The full guideline is available at http://www.ada.org/prof/resources/ topics/infective_endocarditis_guidelines.pdf. ■

### *Gonococcal Infections, CDC's Updated Treatment*

The CDC has issued updated treatment recommendations for gonococcal infections and associated conditions due to the high level of resistance of gonorrhea to fluoroquinolones. The agencies Gonococcal Isolate Surveillance Project demonstrates that fluoroquinolone-resistant gonorrhea is continuing to spread and is now widespread


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throughout United States. Therefore, fluoroquinolones such as ciprofloxacin, ofloxacin, or levofloxacin are no longer recommended. Current recommended regimens for gonococcal infections of the cervix, urethra, and rectum are ceftriaxone 125 mg IM and a single dose or cefixime 400 mg orally in a single dose plus treatment for chlamydia if chlamydial infection is not ruled out. Uncomplicated gonococcal infections of the pharynx should be treated with ceftriaxone 125 mg IM plus treatment for chlamydia, if chlamydial infection is not ruled out. Disseminated gonococcal infection should be treated with ceftriaxone 1 g IM or IV every 24 hours. Pelvic inflammatory disease may be treated with parenteral and oral therapy. Parenteral therapy regimens include cefotetan or cefoxitin plus doxycycline or clindamycin plus gentamicin. An alternative regimen is ampicillin/sulbactam plus oral doxycycline. Oral therapy can be considered in women with mild to moderate disease. With the loss of fluoroquinolones, cephalosporins are the mainstay of most regimens. For patients who are highly allergic to cephalosporins, spectinomycin may be considered although it is not generally available in this country. Another option is azithromycin, however, prescribing should be done in consultation with an infectious disease specialist due to concerns over emerging antimicrobial resistance to macrolides. The CDC's full recommendations are available online at www.cdc.gov/std/treatment/2006/updated-regimens.htm. ■

### Head Lice — Malathion First-Line Treatment

Malathion should be first-line treatment for children who have lice according to a new review in the journal *Pediatrics*. Head lice have become resistant to nearly all first-line treatments in United States including permethrin, which has been considered first-line treatment for years. Malathion, in the formulation containing isopropyl alcohol and terpineol, is safe and effective for lice and all existing points within the life cycle, and generally requires a single treatment, reducing the duration of infestation, and lost time from school and work. Concern about flammability seems to be over emphasized, as there have been no reported cases of bodily injury related to burns (*Pediatrics* 2007. 119:965-974).

### Statins, May Cut the Risk of Cataracts

Statins, the cholesterol wonder drugs, have been associated with a number of other benefits including reduction of inflammation within the arteries, improved bone density, reduction in the risk of colon cancer, renoprotective effects, and reduction in the risk of Alzheimer's disease and other dementias. Now, a new study suggests that the drugs may also cut the risk of cataracts by 50%. Researchers from Australia reviewed the rate of cataract development in 3,654 elderly patients. After 10 years, after controlling for age, gender and others factors, the hazard ratio for any type of cataract in statin users was 0.52. In subgroups, there was a decreased risk of nuclear cataracts (HR = 0.66) and cortical cataracts (HR =0.76), but neither of these reached statistical significance. The authors conclude that there may be a protective influence of statins on cataracts and this needs to be further explored (*Am J Ophthalmol* 2007; 143:687-689). ■

### FDA Actions

Sanofi Aventis has been approved to produce a vaccine to prevent bird flu in humans. The vaccine against the H5N1 virus will not be produced commercially, but will instead be stockpiled by the U.S. government for distribution in case of the outbreak. The FDA admits that the vaccine is not optimal, requiring a higher dose than normal flu vaccine, and 2 shots which must be given 28 days apart. But until other vaccines are developed, this vaccine will be used as the "interim measure."

The FDA is recommending updating black box warning regarding suicidality in young adults (under age 24) starting on antidepressants, calling for appropriate monitoring and close observation. The new recommendation should also include the statement that there was no increase in suicidality in adults over the age of 24, and a decrease in the risk in adults over the age of 64.

The FDA has approved generic versions of 2 of the most popular drugs of the last decade, Ambien (zolpidem) and Zoloft (sertraline). Zolpidem will be available in 5 mg and 10 mg immediate-release tablets. Thirteen manufactures have received approval to market the product. Sertraline is approved in the 25 mg, 50 mg and 100 mg strengths, and will be produced by Ranbaxy Laboratories.

The FDA has issued a warning about the health risks of dietary supplements touted as sexual enhancement products and treatments for erectile dysfunction that have been distributed under the trade names True Man and Energy Max. Both drugs have been sold throughout United States. Energy Max was found to contain an analogue of sildenafil, the active ingredient in Viagra, while True Man was found to contain an analogue of sildenafil and vardenafil, the active ingredient in Levitra. Both drugs can have serious interactions with nitrates. ■