# INTERNAL MEDICINE ALERT

Providing Evidence-based Clinical Information for 30 Years

*A twice-monthly update of developments in internal and family medicine*

AHC Media LLC Home Page—www.ahcmedia.com

CME for Physicians—www.cmeweb.com


AHC Media LLC

## INSIDE



**Financial Disclosure:**
*Internal Medicine Alert's* editor, Stephen Brunton, MD, is a consultant for Amylin, Novo Nordisk, Shionogi Pharma, Takeda, and Teva; he serves on the speakers bureau of Boehringer Ingelheim, Novo Nordisk, and Teva. Peer reviewer Gerald Roberts, MD, reports no financial relationship to this field of study.

# Is Statin Therapy Ever Indicated in Young Adults?

ABSTRACT & COMMENTARY


***By Harold L. Karpman, MD, FACC, FACP***

*Clinical Professor of Medicine, UCLA School of Medicine*


*Dr. Karpman reports no financial relationship to this field of study.*


***Synopsis:*** *Initiating treatment for hypercholesterolemia at age 30 years instead of age 60 years might very well prevent not just 30% of the CAD events as occurred in the 5-year statin trials, but perhaps as many as 60% of the CAD events lifetime.*


**Source:** Steinberg D. Earlier intervention in the management of hypercholesterolemia: What are we waiting for? *J Am Coll Cardiol* 2010;56:627-629.

Historically, adults younger than 35 years of age who do not have an extremely rare genetic disorder, such as familial hypercholesterolemia, have been considered to be at very low short-term risk of developing coronary artery disease (CAD), and it has been presumed that lipid-lowering therapy at this stage in life is unlikely to provide any short-term or medium-term benefit. In fact, current guidelines for the treatment of high cholesterol in young adults have been conservative, based upon the calculated Framingham 10-year risk score, and recommend drug therapy with statins only if cholesterol levels remain very high after a trial of lifestyle modification.[1] However, recent publications make a persuasive case for changing our guidelines from evaluating only the 10-year Framingham risk score to considering lifetime risk,[2] since the reality exists that most persons will die of coronary artery disease sooner or later. For example, while the 10-year risk for a 40-year-old male with a plasma cholesterol level between 200 and 239 mg/dL is only 5%, the lifetime risk is 43%, confirming the fact that CAD pathology in these hypercholesterolemic young men will progress to the point where 50% or more of them will eventually die of CAD.


VOLUME 32 • NUMBER 20 • OCTOBER 29, 2010 • PAGES 153-160

*INTERNAL MEDICINE ALERT* **IS AVAILABLE ONLINE**
**www.internalmedicinealert.com**

Steinberg carefully points out that, for example, initiating statin treatment at age 30 instead of age 60 might very well prevent not just the 30% of events seen in the 5-year statin trials, but as many as 60% of events. It is well known that CAD starts early,[3] and there is good reason to believe that lowering abnormal lipid levels and treatment of other reversible risk factors, such as cigarette smoking, hypertension, and diabetes mellitus, will significantly reduce the progression and final incidence of the abnormal structural characteristics and plaque composition in the coronary arteries that will result over time in symptomatic CAD.

Up until recently, adequate imaging techniques to easily measure quantitatively the burden of early coronary artery lesions have not been available; however, recent significant improvements in low-dose radiation coronary computed tomographic angiography (CCTA) have given us the ability to detect the presence and quantity of calcified coronary artery plaque (CAC) and, perhaps more importantly, non-calcified coronary artery plaque, which is among the earliest signs of evolving CAD. Preliminary results of a recent and yet unreported study in 40 young type 1 and type 2 diabetic patients have revealed that CCTA provided more complete and earlier identification of disease than did CAC, since noncalcified plaque is frequently the only coronary artery abnormality present in many of these patients, especially early on. Obviously, a larger, carefully controlled trial in diabetic and nondiabetic patients is necessary; however, this trial might have to be 30 years or more in duration and would be extremely difficult to mount both from technical and ethical points of view. Having a non-invasive tool such as low-radiation CCTA available at this time for the evaluation of early, asymptomatic CAD may prove to be extraordinarily valuable from objective and practical points of view to determine which patients should start statin drug and lifestyle therapies in their youth and conceivably even in late childhood since obesity and hyperlipidemia are now also becoming epidemic in children.

The Adult Treatment Panel of the National Cholesterol Education Program's fourth report, due in early 2011, will cover whether and how to expand statin-prescribing strategies. Reducing life-long cumulative exposure to LDL-cholesterol via statin therapy initiated early in life may provide more complete protection against future CAD than can be achieved with initiation later in life;[4] however, we must be cognizant of the possible negative effects of statin therapy in general and in young adults, especially since much of this information is still lacking in the literature. Also, we have to be concerned about the special circumstances of young women who may become pregnant and/or who are breastfeeding and the possible negative psychological effects of "labeling" a young person as being unhealthy or disabled because he/she is taking a pharmaceutical preparation, even though these effects almost certainly will be diminished if adequate education about the benefits of drug treatment is provided.

At the present time, vigorous preventive CAD measures, including statin therapy, appear to be indicated for hyperlipidemic persons of any age if they have an elevated CAC score or abnormal CCTA findings such as noncalcified plaque. While we shouldn't sit back and wait to see what happens to these individuals given our current level of knowledge, we should recognize that these conclusions may be changed after the results of carefully controlled long-term studies, which are currently being performed become available. ■

## References


1. National Cholesterol Education Program, National Heart, Lung, and Blood Institute, National Institutes of Health. Third Report of the Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Available at www.nhlbi.nih.gov/guidelines/cholesterol. Accessed Oct. 11, 2010.
2. Lloyd-Jones DM, et al. Lifetime risk of coronary heart disease by cholesterol levels at selected ages. *Arch Intern Med* 2003;163:1966-1972.
3. Enos WF, et al. Coronary disease among United States soldiers killed in action in Korea; preliminary report. *JAMA* 1953;152:1090-1093.



***Internal Medicine Alert***, ISSN 0195-315X, is published monthly by AHC Media LLC, 3525 Piedmont Rd., NE, Bldg. 6, Suite 400, Atlanta, GA 30305.

**EXECUTIVE EDITOR:** Coles McKagen.
**SENIOR MANAGING EDITOR:** Paula Cousins.

**GST Registration Number:** R128870672.

Periodicals Postage Paid at Atlanta, GA 30304 and at additional mailing offices.

POSTMASTER: Send address changes to ***Internal Medicine Alert***, P.O. Box 740059, Atlanta, GA 30374.





**Back Issues: $21.** Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue's date.





**Subscriber Information**

**Customer Service: 1-800-688-2421.**
**Customer Service E-Mail:** customerservice@ahcmedia.com
**Editorial E-Mail:** paula.cousins@ahcmedia.com
**World-Wide Web:** www.ahcmedia.com

**Subscription Prices**

**United States**
1 year with free AMA Category 1 credits: $319
Add $17.95 for shipping & handling.
(Student/Resident rate: $125)

**Multiple Copies**
Discounts are available for group subscriptions, multiple copies, site-licenses or electronic distribution. For pricing information, call Tria Kreutzer at 404-262-5482.

**Canada**
Add 7% GST and $30 shipping.

**Elsewhere**
Add $30 shipping.

**Accreditation**

AHC Media LLC is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

AHC designates this educational activity for a maximum of *45 AMA PRA Category 1 Credits™*. Physicians should only claim credit commensurate with the extent of their participation in the activity.

*Internal Medicine Alert* has been reviewed and is acceptable for up to 24 Prescribed credits by the American Academy of Family Physicians. AAFP accreditation begins 01/01/07. Term of approval is for one year from this date. Each issue is approved for 1 Prescribed credit. Credit may be claimed for 1 year from the date of each issue. The AAFP invites comments on any activity that has been approved for AAFP CME credit. Please forward your comments on the quality of this activity to cmecomment@aafp.org.

This CME activity is intended for the internist/family physician. It is in effect for 36 months from the date of the publication.

AHC Media LLC

**Questions & Comments**
Please call **Paula Cousins**, Senior Managing Editor, at (404) 262-5488.

4. Forrester JS. Redefining normal low density lipoprotein cholesterol: A strategy to unseat coronary disease as the nation's leading killer. *J Am Coll Cardiol* 2010;56: 630-636.

# What's Best for the Breast?

ABSTRACT & COMMENTARY

***By Barbara A. Phillips, MD, MSPH***

*Professor of Medicine, University of Kentucky; Director, Sleep Disorders Center, Samaritan Hospital, Lexington*

*Dr. Phillips is a consultant for Cephalon, and serves on the speakers for Resmed and Respironics.*

***Synopsis:*** *In a very large Norwegian study, use of screening mammography was associated with a reduction in the rate of death from breast cancer, but the screening itself accounted for only about a third of the total reduction in death rate.*

**Source:** Kalager M, et al. Effect of screening mammography on breast-cancer mortality in Norway. *N Engl J Med* 2010;363:1203-1210.

This paper is largely the product of an analysis of the Cancer Registry of Norway, which conducts a breast cancer screening program. As part of this program, all women in the country between the ages of 50 and 69 years have been offered screening mammography every 2 years since 2005. In addition, the breast cancer program required the establishment of multidisciplinary breast cancer management teams and breast units in all of the 19 counties in Norway; these teams consist of radiologists, radiologic technologists, pathologists, surgeons, oncologists, and nurses who manage the care of all breast cancer patients. Overall, about three-fourths of the women who were invited chose to participate in the program. The screening mammograms included two views, which were independently read by two radiologists.

For purposes of this analysis, the authors defined four groups of women with breast cancer: two current groups (diagnosed between 1995 and 2005), some of whom had undergone screening (screening group) and some who had not (nonscreening group), and two historical-comparison groups (diagnosed between 1986 through 1995), before screening was offered.

Based on the timing of implementation of the screening program in each county, the authors grouped the 19 counties into six regions; each county within a given region entered the program at approximately the same time. Death rates were calculated separately for each region. First, the authors compared women in the nonscreening groups with their historical counterparts to determine changes in mortality that most likely resulted from improved treatment and earlier clinical diagnosis. Then they compared women in the screening group with their historical counterparts to determine the change in mortality after implementation of the screening program. In this second comparison, the difference in the rate of death between the two groups was attributed both to the screening program and to improved treatment, so the reduction in mortality that was related to the screening program was the difference between the rate ratio for death among women in the screening group as compared with their historical counterparts and the rate ratio for death among women in the nonscreening group as compared with their historical counterparts.

The investigators estimated rates of death from breast cancer in the four study groups according to the age at diagnosis (20-49 years, 50-69 years, and 70-84 years).

A total of 40,075 women were first diagnosed with breast cancer between 1986 and 2005. During the follow-up period, 4791 of these women (12%) died from breast cancer. Of the women who died, 423 (9%) had received the diagnosis after the introduction of the screening program. The average time of follow-up (from diagnosis) was 2.2 years, with a maximum of 8.9 years. Among women between the ages of 50 and 69 years (the age group that was offered mammography), 6967 received a diagnosis of breast cancer between 1986 and 1995, as compared with 12,056 who received the diagnosis between 1996 and 2005. In the latter group, for women between the ages of 50 and 69 years in the screening group, the rate of death was 18.1 per 100,000 person-years, as compared with 25.3 per 100,000 person-years among their historical counterparts, for a difference of 7.2 deaths per 100,000 person-years (a relative reduction of 28%).

Among women in the nonscreening group, the rate of death was 21.2 per 100,000 person-years, as compared with 26.0 per 100,000 person-years among their historical counterparts, for a difference of 4.8 deaths per 100,000 person-years, a relative reduction of 18%.

When the authors factored in the reduction in mortality among women in the nonscreening group, as compared with their historical counterparts, the relative reduction among women in the screening group was 10%. The authors concluded that since the differences between the current groups and historical groups were 7.2 deaths per 100,000 person-years in the screening group and 4.8 deaths per 100,000 person-years in the nonscreening group, only the overall between-group difference — 2.4 deaths per 100,000 person-years could be attributed to the screening program alone, representing a third of the total

estimated reduction in mortality (2.4 of 7.2).

Among women between the ages of 50 and 69 years in the screening group, those with stage I tumors had a relative reduction in mortality of 16% compared to historical counterparts; among women in the nonscreening group, the corresponding reduction was 13%. Among women with stage II tumors, those in the screening group had a marked 29% reduction in mortality compared to their historical counterparts; among women in the nonscreening group, the reduction was 7%. Among women with stage III or IV tumors, the improvement in prognosis was similar with and without the screening program.

Among women who were not eligible for screening because they were younger than 50 years of age or older than 69 years of age, there was also a significant reduction in the rate of death from breast cancer compared to historical counterparts; the authors attributed this reduction to multidisciplinary breast-cancer management teams. Among women younger than the age of 50 years, there was a nonsignificant relative increase in mortality of 4% ($P = 1.00$) after the introduction of the screening program. Among women who were 70 years of age or older, the relative reduction in mortality of 8% ($P = 0.09$) could be attributed to the establishment of multidisciplinary teams in the screening program.

The authors concluded, "…the take-home message is that breast-cancer screening was associated with an absolute reduction of 10 percentage points in the rate of death from breast cancer. However, the screening program accounted for only one third of the total reduction in mortality … For women between the ages of 50 and 69 years, it was impossible to determine whether the reduction in mortality resulted from earlier diagnoses associated with screening mammography or from the management of treatment by an interdisciplinary team. To our surprise, the reduction in breast-cancer mortality among women between the ages of 70 and 84 years was largely the same as that in the screening group."

## ■ COMMENTARY

First of all, the good news is that breast cancer mortality is most definitely falling. The issue here is whether or not mammography screening contributes significantly enough to improved survival to justify the cost, stress, radiation exposure, and false-positives. An analysis in the United States of breast cancer death from 1975 through 2000 concluded that only about half the observed reduction in mortality resulted from mammography; the rest was attributed to better management of the disease after diagnosis.[1] This current report, indicating that the contribution to reduced death from breast cancer from mammography is only about a third of the total overall reduction, adds considerably to the ongoing debate about screening in general, and breast cancer screening in particular. It confirms that the benefit from screening, compared to post-diagnosis care, is small.

Another issue with regard to screening relates to which age groups are most likely to benefit from mammography. About a decade ago, the World Health Organization recommended screening mammography for women between the ages of 50 and 68 years, based on data suggesting a 25% reduction in death rates from breast cancer with this approach.[2,3] Indeed, based on that recommendation, the approach in Norway (the source of the current paper) has been to offer mammography only to those in that age group. Not so in the United States where mammography has been advocated and offered to women older than age 40. However, nearly a year ago, the U.S. Preventive Services Task Force (USPSTF) recommended against routine screening mammography in women aged 40-49 years, and recommended biennial (rather than annual) screening mammography for women between the ages of 50 and 74 years.[4] It also concluded that evidence is insufficient to assess the additional benefits and harms of screening mammography in women 75 years or older.

Now, after years spent trying to get women to undergo mammograms, clinicians have found themselves backpedalling in the wake of this USPSTF recommendation. The current report from Norway seems to indicate the benefits of screening, even in the 50- to 69-year-old group, may be slim.

So, what should we tell our patients? Perhaps the most important message here is that we cannot afford to be dogmatic about breast cancer screening (or anything else, for that matter). This is clearly not yet a black and white issue. The possible benefits of screening need to be carefully balanced against the very real negatives, including cost, angst, radiation exposure, and unnecessary follow-up testing due to false-positives. ■

## References


1. Berry DA, et al. Effect of screening and adjuvant therapy on mortality from breast cancer. *N Engl J Med* 2005;353:1784-1792.
2. Miller AB, et al. Canadian National Breast Screening Study: 2. Breast cancer detection and death rates among women aged 50 to 59 years. *CMAJ* 1992;147:1477-1488.
3. Nystrom L, et al. Breast cancer screening with mammography: Overview of Swedish randomised trials. *Lancet* 1993;341:973-978.
4. U.S. Preventive Services Task Force. Screening for breast cancer: U.S. Preventive Services Task Force recommendation statement. *Ann Intern Med* 2009; 151:716-726, W-236.

# Could that Persistent Cough Be Pertussis? Don't Rely on the Whoop

ABSTRACT & COMMENTARY

***By Joseph E. Scherger, MD, MPH***

*Clinical Professor, University of California, San Diego*

*Dr. Scherger reports no financial relationship to this field of study.*

***Synopsis:*** *A systematic review shows that the three classical symptoms of paroxysmal cough, post-tussive emesis, and inspiratory whoop are helpful for the diagnosis, but cannot be relied upon to rule in or rule out pertussis as the cause of a chronic cough.*

**Source:** Cornia PB, et al. Does this coughing adolescent or adult patient have pertussis? *JAMA* 210;304:890-896.

Pertussis continues as a major cause of respiratory infection in the United States among children and adults. Pertussis should be considered in any patient with a persistent and prominent cough. The natural history of the infection has three phases. After a 7- to 10-day incubation period, the catarrhal phase is much like a common cold and lasts 1-2 weeks. The presence of mild cough early may make the clinician suspicious for pertussis. Two early symptoms that may be clinically useful are excessive lacrimation and conjunctival injection.

The paroxysmal phase begins during the second week of the illness and the hallmark symptom is coughing spells. A paroxysm is a series of coughs during a single expiration. The cough paroxysm causes low lung volumes, leading to a vigorous inspiration that may result in a whoop, particularly in infants and children who have a smaller trachea. Other classic symptoms that may be present are post-tussive emesis or syncope. The paroxysmal phase may last for 2-3 months.

The final phase of the illness is a persistent cough that becomes progressively milder. The Chinese name for pertussis is "the 100 day cough." Sputum production is not a hallmark of pertussis, so the presentation may be very similar to a viral bronchitis or pneumonia.

*Bordetella pertussis* is a gram-negative coccobacillus and is readily transmitted in respiratory secretions. Diagnosis is not easy and is most commonly made from a culture or direct staining of a properly obtained nasopharyngeal specimen. Specimens must be collected from the ciliated respiratory epithelium of the posterior nasopharynx and not the anterior nares or throat. Serum antibody testing is also done, but is not generally useful with the management of an acute infection.

Macrolide antibiotics such as erythromycin, azithromycin, and clarithromycin are the treatment of choice. Trimethoprim-sulfamethoxazole is an alternative for patients unable to tolerate a macrolide. Early treatment may reduce the severity and duration of the illness, but treatment after the first 1-2 weeks may not have a clinical impact. A principal benefit of treatment is to reduce the contagious period that can last 1 month or longer.

Besides giving an excellent clinical review of pertussis, the study group from the University of Washington and the University of California, San Francisco, did a systematic review of the literature to explore the utility of the classic symptoms. They identified five prospective studies as useful. They found that the presence of post-tussive emesis or inspiratory whoop increases the likelihood of pertussis by about two times. The absence of paroxysmal cough or post-tussive emesis decreased the likelihood of pertussis by about two times. Calculating the sensitivity and specificity of the classic symptoms shows that paroxysmal cough is present in close to 100% of patients with pertussis, but is only about 25%-30% specific. Inspiratory whoop is present in 26%-50% of patients with pertussis and is about 75% specific. Post-tussive emesis is present in 33%-70% of patients with pertussis and is about 70% specific.

## ■ COMMENTARY

The differential diagnosis of chronic cough is a major challenge in primary care. Besides a lower respiratory infection, conditions such as asthma and GERD must be considered. Careful history can usually help us sort out the patients with a respiratory infection. The next challenge is sorting out which infections are likely viral and which are bacterial in origin. Without colored sputum as a prominent symptom, "atypical" bacteria such as *Chlamydia pneumoniae* and *Mycoplasma pneumoniae* are also considered. We need to add pertussis to the list of common possibilities. Fortunately, all respond to macrolide antibiotics, and all three usually resolve eventually without treatment in generally healthy persons.

What do I use to guide whether I am going to use an antibiotic in the presence of a persistent and paroxysmal cough? The severity of the cough and the presence of physical findings will tip me to using an antibiotic. I tell every patient that the illness could be viral, and that the treatment may have no impact on the recovery from the illness, and that they will recover or I want to hear from them. I find on-line communication with patients to be useful to monitor the course and recovery from these common infections.

This article provides a wonderful clinical update on

pertussis and useful clinical research information for diagnosis. Immunization remains the most important public health intervention and we must remember how lethal pertussis can be, especially to infants and young children. ■

## *Pharmacology Update*

# Pegloticase Injection (Krystexxa™)


***By William T. Elliott, MD, FACP, and James Chan, PharmD, PhD***

*Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.*

*Drs. Elliott and Chan report no financial relationship to this field of study.*


A RECOMBINANT, POLYETHYLENE GLYCOL (PEG) MAMMALIAN urate oxidase (uricase) has been approved by the FDA for treatment of hyperuricemia. Uricase metabolizes urate to allantoin, a water-soluble metabolite, which is cleared renally. Pegliticase is marketed by Savient Pharmaceuticals as Krystexxa™.

### Indications

Pegliticase is indicated for the treatment of symptomatic hyperuricemia.[1]

### Dosage

The recommended dose of pegloticase is 8 mg given as an intravenous infusion every 2 weeks. Patients should be premedicated with an antihistamine and corticosteroids, and serum uric acid levels should be monitored before each infusion.[1] Gout flare prophylaxis with a nonsteroidal anti-inflammatory drug or colchicines is recommended starting at least 1 week before initiation of therapy.[1]

Pegloticase is available as an 8 mg vial.

### Potential Advantages

Pegloticase reduced urate levels and resolved at least one target tophus in about 40% of patients that were refractory to conventional antigout drugs.

### Potential Disadvantages

In a clinical trial, anaphylaxis was reported with a frequency of 6.5%. Infusion reactions occurred in 26% of pa-

United States Postal Service
**Statement of Ownership, Management, and Circulation**

| 1. Publication Title | 2. Publication No. | 3. Filing Date |
|---|---|---|
| Internal Medicine Alert | 0 1 9 5 - 3 1 5 X | 10/01/10 |
| 4. Issue Frequency | 5. Number of Issues Published Annually | 6. Annual Subscription Price |
| Semi-Monthly | 24 | $319.00 |

7. Complete Mailing Address of Known Office of Publication *(Not Printer) (Street, city, county, state, and ZIP+4)*: 3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, Fulton County, GA 30305 — Contact Person: Robin Salet; Telephone: 404/262-5489

8. Complete Mailing Address of Headquarters or General Business Office of Publisher *(Not Printer)*: 3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, GA 30305

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor *(Do Not Leave Blank)*

Publisher *(Name and Complete Mailing Address)*: Robert Mate, President and CEO, AHC Media LLC, 3525 Piedmont Road, Bldg. 6, Ste. 400, Atlanta, GA 30305

Editor *(Name and Complete Mailing Address)*: Paula Cousins, same as above

Managing Editor *(Name and Complete Mailing Address)*: Coles McKagen, same as above

10. Owner *(Do not leave blank. If the publication is owned by a corporation, give the name and address of the corporation immediately followed by the names and addresses of all stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, give the names and addresses of the individual owners. If owned by a partnership or other unincorporated firm, give its name and address as well as those of each individual. If the publication is published by a nonprofit organization, give its name and address.)*

| Full Name | Complete Mailing Address |
|---|---|
| AHC Media LLC | 3525 Piedmont Road, Bldg. 6, Ste 400 |
| | Atlanta, GA 30305 |

11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box → ☐ None

| Full Name | Complete Mailing Address |
|---|---|
| Thompson Publishing Group Inc. | 805 15th Street, NW, 3rd Floor |
| | Washington, D.C. 20005 |

12. Tax Status *(For completion by nonprofit organizations authorized to mail at nonprofit rates.) (Check one)*
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☐ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months *(Publisher must submit explanation of change with this statement)*

PS Form **3526**, September 1998 *See instructions on Reverse)*

13. Publication Name: Internal Medicine Alert — 14. Issue Date for Circulation Data Below: August 30, 2010

| 15. Extent and Nature of Circulation | | | Average No. of Copies Each Issue During Preceding 12 Months | Actual No. Copies of Single Issue Published Nearest to Filing Date |
|---|---|---|---|---|
| a. Total No. Copies *(Net Press Run)* | | | 1904 | 1912 |
| b. Paid and/or Requested Circulation | (1) | Paid/Requested Outside-County Mail Subscriptions Stated on Form 3541. *(Include advertiser's proof and exchange copies)* | 1640 | 1418 |
| | (2) | Paid In-County Subscriptions *(Include advertiser's proof and exchange copies)* | 0 | 0 |
| | (3) | Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Non-USPS Paid Distribution | 46 | 46 |
| | (4) | Other Classes Mailed Through the USPS | 44 | 39 |
| c. Total Paid and/or Requested Circulation *(Sum of 15b(1) and 15b(2)* | | | 1730 | 1503 |
| d. Free Distribution by Mail *(Samples, Complimentary and Other Free)* | (1) | Outside-County as Stated on Form 3541 | 37 | 33 |
| | (2) | In-County as Stated on Form 3541 | 0 | 0 |
| | (3) | Other Classes Mailed Through the USPS | 0 | 0 |
| e. Free Distribution Outside the Mail *(Carriers or Other Means)* | | | 22 | 20 |
| f. Total Free Distribution *(Sum of 15d and 15e)* | | | 59 | 53 |
| g. Total Distribution *(Sum of 15c and 15f)* | | | 1789 | 1556 |
| h. Copies Not Distributed | | | 115 | 356 |
| i. Total *(Sum of 15g, and h.* | | | 1904 | 1912 |
| Percent Paid and/or Requested Circulation *(15c divided by 15g times 100)* | | | 97% | 97% |

16. Publication of Statement of Ownership: Publication required. Will be printed in the October 29,2010 issue of this publication. ☐ Publication not required.

17. Signature and Title of Editor, Publisher, Business Manager, or Owner: President and CEO — Date: 9/27/10

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including multiple damages and civil penalties).

**Instructions to Publishers**

1. Complete and file one copy of this form with your postmaster annually on or before October 1. Keep a copy of the completed form for your records.
2. In cases where the stockholder or security holder is a trustee, include in items 10 and 11 the name of the person or corporation for whom the trustee is acting. Also include the names and addresses of individuals who are stockholders who own or hold 1 percent or more of the total amount of bonds, mortgages, or other securities of the publishing corporation. In item 11, if none, check the box. Use blank sheets if more space is required.
3. Be sure to furnish all circulation information called for in item 15. Free circulation must be shown in items 15d, e, and f.
4. Item 15h., Copies not Distributed, must include (1) newsstand copies originally stated on Form 3541, and returned to the publisher, (2) estimated returns from news agents, and (3), copies for office use, leftovers, spoiled, and all other copies not distributed.
5. If the publication had Periodicals authorization as a general or requester publication, this Statement of Ownership, Management, and Circulation must be published; it must be printed in any issue in October or if the publication is not published during October, the first issue printed after October.
5. In item 16, indicate date of the issue in which this Statement of Ownership will be published.
6. Item 17 must be signed.

***Failure to file or publish a statement of ownership may lead to suspension of second-class authorization.***

PS Form **3526**, September 1999 *(Reverse)*

tients that received pegloticase compared to 5% for placebo. Patients that receive retreatment may be at increased risk of anaphylaxis and infusion reactions.[1] Anti-pegloticase antibodies have been detected in 92% of patients treated with pegloticase and high titers have been associated with treatment failure and a higher incidence of infusion reactions. Pegloticase is contraindicated in patients with glucose-6-phosphate dehydrogenase deficiency.

**Comments**

Pegloticase is a pegylated recombinant modified mammalian uricase product produced by *Escherichia coli*. The half-life is 1-2 weeks compared to 24 hours for the previously approved recombinant uricase, rasburicase.[2] Efficacy was shown in two randomized, double-blind, placebo-controlled, 6-month studies in subjects with chronic gout with either treatment failure or contraindication to allopurinol.[1] The study population had a mean age of 55 years, mean baseline serum urate level of 10 mg/dL, and symptomatic gout with at least three gout flares in the previous 18 months or at least one gout tophus or gouty arthritis; 82% were male. Subjects were randomized 2:2:1 to pegloticase 8 mg every 2 weeks, 8 mg every 4 weeks, or placebo. The primary endpoint was plasma urate levels below 6 mg/dL for 80% of the time in months 3 and 6. The secondary endpoint was response of tophi defined as 100% resolution of at least one target tophus, appearance of no new tophi, and no single tophus showing progression. In the first study, 47% of subjects (n = 104) randomized to 8 mg every 2 weeks met the primary endpoint compared to 20% for 8 mg every 4 weeks and 0% for placebo. In the second study, response rates were 38%, 49%, and 0%, respectively. In a pooled analysis, 45% of subjects on the high dose met criteria for the secondary endpoint compared to 26% for the lower dose and 8% for placebo. Reduction in urate levels can be observed within 6 hours.[3] The most common adverse events were infusion reactions (26% vs 5% for placebo), nausea (12% vs 2%), and contusion or ecchymosis (11% vs 5%). Gout flares were reported in 77% of subjects in the clinical trials.

**Clinical Implications**

Gout is a common disorder that affects about 1% of adults and is much more prevalent in men.[4] Chronic hyperuricemia (> 7 mg/dL) increases the risk of gout and may be an independent risk factor for renal and cardiovascular disease. Pegloticase provides another option for patients with hyperuricemia that have not adequately responded to standard therapy (e.g., allopurinol, febuxostat). It is successful in maintaining uric acid level below 6 mg/dL in about 40% of treatment refractory patients. ■

**References**


1. Krystexxa Prescribing Information. East Brunswick, NJ: Savient Pharmaceuticals; September 2010.
2. Burns CM, Wortmann RL. Gout therapeutics: New drugs for an old disease. *Lancet* 2010 Aug 16; Epub ahead of print.
3. Sundy JS, et al. Reduction of plasma urate levels following treatment with multiple doses of pegloticase (polyethylene glycol-conjugated uricase) in patients with treatment-failure gout: Results of a phase II randomized study. *Arthritis Rheum* 2008;58:2882-2891.
4. Saag KG, Choi H. Epidemiology, risk factors, and lifestyle modifications for gout. *Arthritis Res Ther* 2006;8(Suppl 1):S2.




# *CME Questions*

**53. Statin drug therapy:**

a. should never be used in persons younger than age 30.
b. may be administered carefully to pregnant and/or breast-feeding women.
c. should be considered for all individuals regardless of age if they demonstrate noncalcified coronary artery plaque on CCT and/or have a significantly abnormal CAC burden.
d. should be reserved for patients with hemodynamically significant CAD.

**54. Breast cancer mortality:**

a. continues to rise despite major expenditures in screening and care.
b. appears not to be affected by post-diagnosis clinical care.
c. is influenced mostly by regular use of screening mammography.
d. has fallen for all age groups of women.

**55. Which clinical symptom is most commonly present in adults with pertussis, assisting in diagnosis?**

a. Inspiratory whoop
b. Post-tussive emesis
c. Paroxysmal cough
d. Yellow sputum

**Answers:** 53. c, 54. d, 55. c.

*By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville*
*Dr. Kuritzky is a consultant for Abbott, AstraZeneca, Boehringer Ingelheim, Daiichi, Sankyo, Forest Pharmaceuticals, Lilly, Novo Nordisk, Takeda.*

## Once weekly exenatide vs sitagliptin or pioglitazone for type 2 diabetes

**Source:** Bergenstal RM, et al. Efficacy and safety of exenatide once weekly versus sitagliptin or pioglitazone as an adjunct to metformin for treatment of type 2 diabetes (DURATION-2): A randomised trial. *Lancet* 2010; 376:431-439.

The incretin class of medications (exenatide, liraglutide, sitagliptin, saxagliptin) all share the favorable quality of not being associated with weight gain. Recently published data support the efficacy, tolerability, and simplicity of once-weekly exenatide. Bergenstal et al compared exenatide once weekly (EXEN-W) with sitagliptin (STG) or pioglitazone (PIO) as add-on therapy for persons with type 2 diabetes (n = 491) who had not attained goal with metformin.

At the end of 26 weeks, several outcomes favored EXEN-W. A1c on EXEN-W was 0.6% lower than STG, and 0.3% lower than PIO. Weight loss was also greatest in the EXEN-W group. Adverse effect profiles with each treatment arm were consistent with prior trials, and the discontinuation rate was similar for each group.

EXEN-W reduced systolic BP more than sitagliptin, but similarly to pioglitazone. Favorable lipid effects were seen with each treatment arm: The greatest increase in HDL was seen with pioglitazone.

As clinicians make their therapeutic choices for diabetes management, the relevance of medication impact upon CV risk factors such as BP, weight, and lipids merits our consideration. ■

## Prevalence of hearing loss in U.S. adolescents

**Source:** Shargorodsky J, et al. Change in prevalence of hearing loss in U.S. adolescent. *JAMA* 2010;304:772-778.

My grandmother always claimed that listening to loud rock and roll music would be the demise of my hearing … but I still don't know if she was right. In those days we used to listen to something called a record player (younger clinicians interested to see such an archaic device can readily locate one on Google), and I have always wondered whether those cars bouncing up and down at the traffic light next to me, loaded with rap music, would be determined to be similarly ototoxic, or worse. Well, if the NHANES data are correct, we still don't know.

According to this analysis of data from NHANES, the prevalence of hearing loss has increased when one compares the 1988-1994 interval with 2005-2006. Indeed, the relative risk of any hearing loss (induced by any factor) has increased by more than 30%.

Hearing loss was associated with poverty and a history of > 3 ear infections, but not exposure to persistent (> 5 hrs/week) loud noise or firearm use. In support of grandma's point of view, a recent study from Australia noted hearing loss 70% more often in teens who had used personal stereo devices.

Overall, the prevalence of any hearing loss increased from 11.1% to 14.0% over the decade studied; further elucidation of modifiable risk factors would be helpful. ■

## Postoperative abdominal wall hernias: Best repair methodology

**Source:** Itani KM, et al. What to advise patients about hernias. *Arch Surg* 2010;145:322-328.

The literature indicates that almost one-fourth of persons who undergo abdominal surgery will subsequently incur an abdominal wall hernia. The optimum method for repairing such hernias has not been established. Itani et al performed a randomized trial of laparoscopic vs open repair of ventral incisional hernias at four Veterans Affairs hospitals (n = 162).

There was a substantial risk reduction for complications in the laparoscopic group vs the open repair group (absolute incidence = 31.5% vs 47.9%). In particular, surgical wound site infection was almost 4-fold less in the laparoscopic group. Pain scores at 1 year were less in the laparoscopic group, and return to work was quicker. The only major advantage of open surgical treatment was the incidence of major complications, primarily bowel injury (4.4% in the laparoscopic group vs 1.4% in the open surgery group). One additional advantage of open surgical repair was a trend toward lower recurrence in this group (8.2% vs 12.5%; *P* = NS).

In general, asymptomatic incisional ventral hernias do not require repair, but once they are symptomatic, laparoscopic surgery shows distinct advantages. The surgeons in this trial had not performed a high volume of laparoscopic procedures; hence, clinicians might anticipate even better outcomes as experience accrues. ■

**In Future Issues:** Fat-free Milk and Chronic Constipation