Which fractures are associated with osteoporosis?

Osteoporosis is a skeletal disorder characterized by compromised bone strength and a tendency toward fractures. Osteoporotic fractures can occur throughout the body. Vertebral fractures are the most common, while hip fractures are the most costly in terms of medical expenses, morbidity, and mortality. Approximately 20% of patients with a new hip fracture will die within the year and more than 50% will never regain their prior functional capacity.1

The social and economic burden of osteoporotic fractures is increasing in the United States and worldwide as the population ages. More than 10 million people currently have osteoporosis in the United States,2 where 1.5 million osteoporotic fractures occur annually.3 Both prevention and the early identification and treatment of the condition are important clinical and public health priorities.

Current osteoporosis guidelines

Current guidelines for the prevention and diagnosis of osteoporosis4 include:

- Advise all patient to consume adequate amounts of vitamin D and calcium.
- Recommend regular weight-bearing exercise and muscle strengthening.
- Emphasize the importance of avoiding tobacco smoking and excessive alcohol intake.
- Recommend bone mineral density (BMD) testing to all women aged 65 years or older.
- Recommend a BMD test to postmenopausal women who have suffered a “fragility” fracture to confirm the diagnosis and determine the severity of the condition.
- Initiate therapy when the BMD T score is 2 standard deviations (SD) below the mean for a healthy adult.

Markers for osteoporosis

The term “fragility” or “low-trauma” fracture is generally applied to fractures that are caused by a fall from a standing height or less.
As these guidelines indicate, they are considered to be markers for osteoporosis. In contrast, it is widely believed, with little supporting evidence, that “high-trauma” fractures (eg, as might occur in auto accidents or falls from a roof or ladder) are not related to underlying bone health. Consequently, many people with high-trauma fractures are not worked up for osteoporosis, and “high-trauma” fractures are not tracked as outcomes in osteoporosis studies.

**Study of fracture type and BMD**

To better assess the relationship between bone health, fractures, and types of trauma, researchers followed 2 large cohorts of primarily white, community-dwelling adults aged 65 or older. One cohort, with 8,022 women, was derived from the Study of Osteoporotic Fractures and had a mean follow-up of 9.1 years. A second cohort, with 5,995 men, was derived from the Osteoporotic Fractures in Men Study and had a mean follow-up of 5.1 years. Both cohorts excluded people with bilateral hip replacements or who required assistance with ambulation. For the men, BMD was measured at enrollment. BMD was measured in women at their second clinic visit after enrollment.

**High- versus low-trauma fracture**

Patients in both cohorts were contacted every 4 months by mailed questionnaire to determine if they had sustained a nonsynip fracture. When a fracture was reported, that patient was interviewed about events surrounding the injury. Interviewers were blinded to the patient’s BMD. Fractures were classified as high trauma (assault; motor vehicle accident; being struck by a fast-moving projectile; or fall from a roof, chair, ladder, or table) or low trauma (fall from a standing height or less; falls on stairs, steps, or curbs; collisions with stationary objects while ambulating; and other minimal trauma). A 3-member physician panel audited the trauma classifications.

Overall, 264 women and 94 men sustained an initial high-trauma fracture and 3,211 women and 346 men sustained an initial low-trauma fracture. Among women, most of the high-trauma fractures were due to motor vehicle crashes. Among men, similar proportions of high-trauma fractures were due to sporting injuries; falls from ladders, roofs, and trees; and motor vehicle crashes. Rib and wrist fractures were the most common high-trauma fractures for both men and women.

**Both types of fractures were associated with low BMD**

The key finding was that both types of fractures were associated with a low BMD. For women, for each 1 SD reduction in hip BMD there was an increased risk of both high-trauma fracture (multivariate relative hazard [RH] 1.45; 95% confidence interval [CI], 1.23–1.72) and low-trauma fracture (RH 1.49; 95% CI, 1.42–1.57). The same was true in men: Each –1 SD in hip BMD was associated with an increased risk of both high-trauma and low-trauma fractures (RH 1.54; 95% CI, 1.20–1.96; and RH 1.69; 95% CI, 1.49–1.91, respectively). The risk of subsequent fracture was 34% greater (95% CI, 7%–67%) in women with an initial high-trauma fracture and 31% greater (95% CI, 20%–40%) in women with an initial low-trauma fracture compared with women without fractures. (The risk of subsequent fracture was not modeled in men.)

**Study weaknesses**

This study had several weaknesses, including (1) lack of information on spinal fractures, (2) the introduction of bisphosphonate therapy during the research (which had the potential for biasing results primarily in the women’s cohort), (3) inclusion of a relatively healthy, primarily white patient panel, and (4) not controlling for a history of prior falls, a known risk for future fractures.

Nevertheless, these findings highlight that the common method of clinically predicting underlying bone density based on the fracture history is flawed. In retrospect, it is easy to appreciate that patients cannot accurately describe the magnitude of forces applied to their bones, and many details about load and strain are lost in simple descriptions of collisions of people and their environment.

**Bottom line**

Therefore, the evidence suggests that physicians should consider all fractures in older adults as red flags for osteoporosis. Although no cost-effectiveness studies of this strategy have been published, an older patient with any fracture should probably receive counseling about adequate exercise,
dietary advice about calcium and vitamin D intake, and be offered a BMD study.

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REFERENCES

Evidence-Based Medicine Ratings
Evidence-Based Practice utilizes a simplified rating system known as the “Strength of Recommendation Taxonomy” (SORT).

1 Strength of Recommendation (SOR) ratings are given as key recommendations for readers. SORs should be based upon the highest quality evidence available.
   A. Recommendation based on consistent and good-quality patient-oriented evidence
   B. Recommendation based on inconsistent or limited-quality, patient-oriented evidence
   C. Recommendation based on consensus, usual practice, opinion, disease-oriented evidence, or case series for studies of diagnosis, treatment, prevention, or screening

2 Levels of Evidence (LOE) determine whether a study measuring patient-oriented outcomes is of good or limited quality, and whether the results are consistent or inconsistent between studies.
   Study quality
   1. Good-quality, patient-oriented evidence (eg, validated clinical decision rules, systematic reviews, and meta-analyses of randomized controlled trials [RCTs] with consistent results, high-quality RCTs, or diagnostic cohort studies)
   2. Lower-quality, patient-oriented evidence (eg, unvalidated clinical decision rules, lower-quality clinical trials, retrospective cohort studies, case control studies, case series)
   3. Other evidence (eg, consensus guidelines, usual practice, opinion, case series for studies of diagnosis, treatment, prevention, or case series)

3 Consistency across studies
   Consistent – Most studies found similar or at least coherent conclusions (coherence means that differences are explainable); or if high-quality and up-to-date systematic reviews or meta-analyses exist, they support the recommendation.
   Inconsistent – Considerable variation among study findings and lack of coherence; or if high-quality and up-to-date systematic reviews or meta-analyses exist, they do not find consistent evidence in favor of the recommendation.

Important questions

Dear EBP Readers,

Recently, I had the privilege of retaking the board exam in family medicine. I drove to a children’s learning center located in a shabby strip mall, sat before one of their beige computer stations for 6 hours, and answered 350 multiple choice questions that would determine if I am still qualified to be a family physician. At a price of $3.29 per question, the experience got me thinking about what questions are really important to being a practicing physician.

With one’s livelihood hanging in the balance, board questions are certainly important. But their primary importance is to society. Should I one day become senile and not have the good sense to retire, my plummeting board scores will surely alert the authorities. Reflecting this function, it was clear by question 53 that the exam was going to stick to the textbook basics. (Note to ABFM: I hope that wasn’t supposed to be a secret!)

By question 187, I was contemplating how we work with a completely different, but equally important, set of questions at Evidence-Based Practice. Having mastered the basics, professionals become curious about the rigor behind the basics and how new information should be integrated with the basics. These questions, generated from actual practice, keep the professional (and our newsletter) sharp, engaged, and moving forward.

But by question 326, 5 hours and 48 minutes into my exam, I began to wonder about a third type of question that could never be a part of the board exam, or a part of the newsletter for that matter. I began to ponder Zen-like questions that are critical to a career but can only be answered in essays written by the heart.

• “How can you see when your emotions make it hard for you to see?”
• “How can you tend to your career and your life with equal care?”
• “How can you approach patients, staff, peers, and family every day with reverence?”

Perhaps I had just been staring at a computer screen for too long. But those were the questions that lingered in my mind, driving home after the easy questions were all answered.

Regards,

Jon O. Neher, MD
The HelpDesk Search Strategy

HelpDesk Answers are intended to provide the same quality response to a clinical question as would be achieved by a search-savvy physician spending an hour or so on the Internet. Authors of HelpDesk Answers are required to search PrimeEvidence (http://www.primeanswers.org) and the TRIP database (www.tripdatabase.com). These portals provide access to more than a dozen sources of the highest quality evidence-based clinical information, including BMJ Clinical Evidence, the Guide to Clinical Preventive Services, AHRQ Evidence Reports, and others. Searches of the Cochrane Database, Medline, and other databases are also included, as needed.

What is the best management strategy for patients with renal failure and volume overload who are unresponsive to loop diuretics?

Evidence-Based Answer

Combining loop diuretics with thiazide-type diuretics and continuous infusions of loop diuretics should be tried for patients who are unresponsive to bolus administration of loop diuretics alone. (SOR A, based on guidelines citing homogenous randomized controlled trials.) Other actions that might be considered include fluid restriction, sodium restriction, discontinuing offending medications such as nonsteroidal anti-inflammatory drugs (NSAIDs), ultrafiltration, and hemodialysis. (SOR C, based on expert opinion and disease-oriented outcomes.)

The National Kidney Foundation generated guidelines on use of diuretics in chronic kidney disease. An independent, multidisciplinary working group authored the guideline, assisted by an evidence review team performing an English language Medline literature search. The guidelines were peer-reviewed, but have not been prospectively validated. The guidelines recommend combining a loop diuretic with a thiazide-type diuretic to overcome diuretic resistance, stating that “there is strong evidence that the practice improves health outcomes, and benefits substantially outweigh harms.” Adjunct measures such as sodium restriction and stopping NSAIDs are also recommended, but not evidence-linked or assigned a SOR by the guidelines.

Three other peer-reviewed but not prospectively validated guidelines primarily focus on patients with heart failure (with and without renal failure). A joint guideline from the American College of Cardiology and the American Heart Association was based on an English language literature search of Medline and EMBASE and authored by a writing committee with members from multiple medical organizations. These guidelines recommend discontinuing NSAIDs, assigning it a class I recommendation (treatment is useful/effective) based on nonrandomized or disease-oriented studies. Other recommendations are given, but are not assigned a level of evidence (LOE) or SOR: combining loop diuretics with thiazide-type diuretics, continuous infusion of loop diuretics, fluid restriction, ultrafiltration, and hemodialysis.2

A Department of Veterans Affairs (VA) guideline was based on a literature search using Medline, OVID, and Evidence Based Medicine reviews, and bibliography searches to find English language studies with a focus given to the VA population.3 Written by practicing VA and Department of Defense physicians, these guidelines recommend combining loop and thiazide diuretics for refractory edema, giving it a SOR B (maybe useful/effective).

A guideline developed by the Institute for Clinical Systems Improvement recommends combining loop diuretics with thiazide diuretics and continuous infusion of loop diuretics based on randomized controlled trials. Other recommendations (described as “out of guideline”) for refractory edema included ultrafiltration or hemodialysis. The literature search strategy was not well described.4

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What is the best therapy for molluscum contagiosum?

Evidence-Based Answer
Because most cases of molluscum will spontaneously resolve, watchful waiting is a reasonable option. When therapy is elected, curettage with topical anesthesia is the most effective and is well tolerated. Several topical agents also speed clearing of individual lesions. (SOR B, based on small clinical trials.)

The duration of an individual molluscum lesion and a molluscum viral colonization is highly variable. Crops of molluscum may appear to come and go for several months. However, most colonizations are self-limited, resolving within 6 to 9 months. Thus, watchful waiting is clearly a therapeutic option for patients with an intact immune system.

Four common treatments—curettage, cantharidin, salicylic acid combined with lactic acid, and imiquimod—were studied in a 2006 prospective randomized trial of 124 children aged 1 to 18 years. All participants had between 10 and 100 lesions, but 10 random lesions were chosen for treatment. Curettage (following topical EMLA or lidocaine) and cantharidin therapy were applied in the office. The acid combination and imiquimod were applied at home, beginning 3 times weekly, with progression to daily. Parents brought their children for repeat visits at 7, 21, 84, and 120 days if any lesions remained.

With a single course of treatment, complete resolution was achieved in 80% of patients treated with curettage, 37% with cantharidin, 53% with the acid combination, and 55% with imiquimod. Curettage was the best tolerated overall. Cantharidin led to blisters. The acid combination had the lowest rate of satisfaction due to irritation. Topical imiquimod, while fairly effective, required an extended dosing schedule. This study was limited in that a placebo group was not included.

A 2004 double-blind randomized trial involved 23 children aged 1 to 9 years with non-genital lesions. Participants had between 10 and 60 lesions (average 27). The patients were randomized to imiquimod 0.5% cream or vehicle. The cream was applied by parents 3 times weekly for 12 weeks, during which time patients were seen biweekly. At 4 weeks, partial clearance, defined as resolution of >30% of the lesions, was seen in 58% of imiquimod patients and 0% of vehicle patients. Complete clearance at 12 weeks was noted in 33% of imiquimod patients and 9% of vehicle patients (P=.0361). Both groups had similar rates of associated pruritus, but 58% of imiquimod patients noted erythema, compared with 22% of vehicle patients.

A 1994 randomized controlled trial randomized 150 individuals aged 10 to 26 years to podophyllotoxin 0.5% cream, podophyllotoxin 0.3% cream, or placebo. Participants had 1 to 20 lesions (average 7.5), located primarily on the face, inner thighs, abdomen, and genitalia. Participants self-administered the medication twice daily for 3 days, and then repeated this treatment weekly for 3 additional weeks. At 1 month, the first group had a 92% cure rate, the second group had a 52% cure rate, and the placebo group had a 16% cure rate (P<.001). Patients were examined weekly for 12 weeks, then monthly until 6 months. None of the lesions recurred during the follow-up period.

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4. Syed TA, Lundin S, Ahmad M. Topical 0.3% and 0.5% podophyllotoxin cream for self-treatment of molluscum contagiosum in males. A placebo-controlled, double-blind study. Dermatology 1994; 189:65–68. [LOE 1b]

Do oral hypoglycemic agents reduce mortality in type 2 diabetes?

Evidence-Based Answer
Metformin reduces all-cause mortality when used to treat patients with type 2 diabetes who are overweight. (SOR A, based on a meta-analysis and large randomized controlled trials [RCTs].) The effect of thiazolidinediones (TZDs) on mortality is less clear (meta-analyses have heterogeneous outcomes), and further studies are warranted.

The United Kingdom Prospective Diabetes Study (UKPDS) was one of the largest and longest prospective trials involving patients with type 2 diabetes. A subset of overweight patients (n=1,704) from the original UKPDS group were enrolled in the UKPDS 34 study. Patients were randomized to intensive therapy with metformin, intensive thera-
py with other agents, or conventional therapy with diet and exercise for an average of 10.7 years.

A significant decrease was noted in all-cause mortality among overweight patients assigned to intensive therapy with metformin compared with patients assigned to diet and exercise (absolute risk reduction 7%; \( P = .011 \)). The metformin group also had a significant reduction in mortality compared with patients taking sulfonylureas or insulin (absolute risk reduction 5.4%; \( P = .021 \)). Based on this latter comparison, 19 overweight diabetic patients would need to be treated with metformin rather than sulfonylureas or insulin for 10.7 years to prevent 1 death.

A Cochrane review of 29 trials (n=5,259) using metformin as first-line therapy for overweight patients with type 2 diabetes concluded that metformin prevents vascular complications and mortality. For obese patients receiving intensive therapy with metformin compared with conventional therapy, there was a statistically significant reduction in diabetes-related death (relative risk [RR]=0.61; 95% confidence interval [CI], 0.4–0.94) and all-cause mortality (RR=0.68; 95% CI, 0.49–0.93). 3

The American Diabetes Association and European Association for the Study of Diabetes consensus guidelines for the management of hyperglycemia in type 2 diabetes include metformin as first-line therapy in all patients without contraindications due to efficacy, safety, and other beneficial effects, including a reduction in macrovascular disease and mortality. 3

The effect of TZDs on mortality in type 2 diabetes is less clear. A recent meta-analysis of 42 trials (n=27,843) compared the use of rosiglitazone with a comparator group (a variety of diabetes regimens that did not include rosiglitazone). The rosiglitazone group was associated with a significantly increased risk of myocardial infarction (odds ratio 1.43; 95% CI, 1.03–1.98). In contrast, a meta-analysis of 19 trials (n=16,390) compared the use of pioglitazone with a comparator group. Pioglitazone use was associated with a decreased risk of the primary outcome, a composite endpoint of death, myocardial infarction, or stroke (hazard ratio [HR] 0.82; 95% CI, 0.72–0.94). However, the reduction was not statistically significant when each of these clinical outcomes was evaluated separately. The group receiving pioglitazone did have a significant increase in heart failure (HR 1.41; 95% CI, 1.19–1.68; \( P = .004 \)). The increased risk of heart failure was not observed among patients with diabetes and congestive heart failure who were not taking pioglitazone.
CI, 1.14–1.76), but without an increase in mortality.

Additional prospective randomized trials are warranted before a definitive conclusion can be made regarding the use of TZDs and the effects on mortality in patients with type 2 diabetes.

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Should we discontinue osteoporosis screening for patients older than 80?

Evidence-Based Answer

The incidence of osteoporosis increases with age, and current guidelines do not advise discontinuing screening because of age. Any decision to stop screening must be made on a case-by-case basis. (SOR C, expert opinion.) The 3-item osteoporosis risk assessment instrument (ORAI) and an online 10-year fracture risk assessment tool by the World Health Organization (WHO) may help identify patients at lower risk for future fractures.

In a large prevalence study of more than 160,000 postmenopausal US women, the rate of undiagnosed osteopenia was 39% and the rate of undiagnosed osteoporosis was 7%. Advancing age was associated with higher rates. Compared with women at age 50, women aged 55 to 59 were somewhat more likely to have osteoporosis (odds ratio [OR] 1.7; 95% confidence interval [CI], 1.56–2.06), whereas women 80 years and older were much more likely to have osteoporosis (OR 22.5; 95% CI, 19.82–25.67).

The American Geriatric Society recommends that women older than 75 be counseled about osteoporosis risk and the pharmacologic prevention of osteoporosis on at least 1 occasion. They also have a position paper on general health screening in the elderly advising against age limits for disease screening and promoting a case-by-case multifaceted approach to screening decisions.

Guidelines from the US Preventive Services Task Force and the American Academy of Family physicians recommend that screening for osteoporosis in women begin at age 65 for those with no risk factors, or at age 60 for women with risk factors. They do not suggest an upper age limit at which screening should stop.

The National Osteoporosis Foundation recently issued new guidelines in which they recommend counseling for osteoporosis risk in both postmenopausal women and men older than 50, combined with bone mineral density screening starting in women at 65 and for men at 70. Again, no upper age limit was suggested at which to stop screening.

The WHO recently made available an online resource to determine 10-year fracture risk, which can be used with or without a bone density score (http://www.shef.ac.uk/FRAX/). This rapid assessment tool takes into account multiple risk factors and can help clinicians determine the need for further screening. Another tool, the ORAI, identifies 3 predictors of low bone density: low weight, no current use of estrogen therapy, and age. This tool has a sensitivity of 93.3% and a specificity of 46.4% (positive likelihood ratio [LR+] 1.7, and LR= 0.14) for identifying patients with a T score of –2.0 SD. The likelihood ratios suggest that the ORAI is best used to identify patients at low risk of fracture.

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HelpDesk

Is red yeast rice a safe and effective alternative to statin drugs for lowering cholesterol?

Evidence-Based Answer

No. Some red yeast rice products contain monacolins, including monacolin K—identical to lovastatin—and may be effective. (SOR B, based on lower quality randomized controlled trials [RCTs].) But as with lovastatin, use of red yeast rice is associated with symptomatic myopathy. (SOR C, based on case reports.) Also, analytical reports have found that many red yeast rice products contain negligible monacolin content. Thus, if effective, red yeast rice is not completely safe; while if the product is safe, it may no longer be effective.

Red yeast rice is a rice product on which the yeast strain Monascus purpureus has been grown and subsequently powdered, encapsulated, and sold as a dietary supplement. A review of 93 RCTs, mostly versus statins or other treatments, included a meta-analysis of 8 placebo-controlled trials (n=689 participants; inclusion criteria, primary hyperlipidemia). The weighted average lipid changes for patients using red yeast rice compared with placebo were –35 mg/dL for total cholesterol, –28 mg/dL for low-density lipoprotein (LDL) cholesterol, –36 mg/dL for triglycerides, and +6 mg/dL for high-density lipoprotein (HDL) cholesterol.

The authors described most of the trials as being of low methodological quality; 91 of the 93 trials were conducted in China and published in Chinese. The 1 trial conducted in the United States was a randomized, placebo-controlled, double-blind study of subjects with primary hyperlipidemia (LDL>160 mg/dL). It reported changes compared with placebo of –35, –33, –13, and 0 mg/dL for total cholesterol, LDL, triglycerides, and HDL, respectively.

Although it comes as no surprise that a monacolin-containing product will lower cholesterol, a risk of adverse effects accompanies the benefits. Case reports have described symptomatic myopathy from use of red yeast rice supplements. Thus, red yeast rice products might be effective, but not completely safe.

Emphasis needs to be placed on “might.” Red yeast rice does not have a definition of composition. In the US trial, the test product was described as 2,400 mg/d of red yeast rice product containing approximately 0.4% monacolins (~10 mg/d).

That test product is no longer commercially available. Most of the products marketed in the United States do not specify monacolin content. In 1 study, an analysis of 9 red yeast rice samples from China revealed a 10-fold range of monacolin content. That study cited earlier reports with similar results, including some commercial product samples with no measurable monacolin content.

The US Food and Drug Administration (FDA) has consistently opposed the marketing of red yeast rice as a dietary supplement. After a contested FDA action initiated in 1998, a US District Court decision was reached in 2001 that red yeast rice products “...that contain lovastatin are subject to regulation as drugs...and are not dietary supplements.” In 2007 the FDA issued warning letters to 2 marketers of red yeast rice products and posted a press release warning consumers to avoid red yeast rice products.

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Maynard, MA

“Evidence based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of evidence based medicine means integrating individual clinical expertise with the best available external clinical evidence from systematic research.”
New ophthalmic antibiotics for bacterial conjunctivitis

The Bottom Line
Zymar®, Vigamox®, and AzaSite® should be reserved for second-line treatment of bacterial conjunctivitis or for patients who do not respond or have contraindications to first-line antibiotics.

Key Points
- Acute bacterial conjunctivitis is often self-limiting or easily treatable
- Broad-spectrum antibiotics may improve patient comfort, hasten rate of recovery, and prevent spread of infection
- Newer ophthalmic antibiotic preparations (Zymar, Vigamox, AzaSite) should not be used first-line for bacterial conjunctivitis due to cost, concern for resistance, and availability of other effective, well-tolerated agents
- Zymar and Vigamox have an established place in therapy for sight-threatening infections, including keratitis and endophthalmitis, and for surgical prophylaxis

The Pitch
Zymar (gatifloxacin 0.3%), Vigamox (moxifloxacin hydrochloride 0.5%), and AzaSite (azithromycin 1%) are new ophthalmic antibiotic preparations approved by the US Food and Drug Administration (FDA) for treatment of bacterial conjunctivitis in adults and children aged 1 year and older. Manufacturers of these products claim rapid and effective protection from bacteria that cause “pink eye” with few, mild adverse effects.1-3

Context
Acute conjunctivitis, commonly known as “pink eye,” is the most common ophthalmologic complaint in primary care. The condition is often self-limiting or easily treatable. Clinical trial data have demonstrated that acute bacterial conjunctivitis usually resolves within 2 to 10 days even without treatment, and serious complications occur infrequently regardless of treatment.4 However, bacterial eradication with broad-spectrum topical antibiotics has been advocated on the grounds that they improve patient comfort, hasten recovery, and may prevent relapse or person-to-person spread.4

Several topical antibiotic ointments and solutions are currently available (Table); while most are relatively inexpensive (~$10), the newer generation fluoroquinolones (Vigamox, Zymar) and AzaSite may cost in excess of $70 for a 3- to 5-mL bottle.

Ophthalmic fluoroquinolone antibiotics have become widely used for the treatment of ocular infections. Both of the fourth-generation agents, gatifloxacin (Zymar) and moxifloxacin (Vigamox), as well as the older fluoroquinolones, ciprofloxacin (Ciloxan), levofloxacin (Quixin), and ofloxacin (Ocuflox), are FDA approved for the treatment of bacterial conjunctivitis. However, due to concerns for bacterial resistance, the general recommendation is to avoid older topical fluoroquinolones. In addition, Zymar and Vigamox should only be used second-line or when first-line agents are contraindicated due to their cost, concern for resistance, and availability of other effective, well-tolerated, less expensive ophthalmic antibiotics. The newer fluoroquinolones have an established place in therapy for serious eye conditions, including keratitis and endophthalmitis, or for surgery prophylaxis. Although FDA indicated for bacterial conjunctivitis and convenient to dose, AzaSite likewise offers little therapeutic advantage with regard to efficacy over first-line agents.

The Data
Few available controlled clinical trials of patients with bacterial conjunctivitis have been conducted with the newer ophthalmic antibiotics. The efficacy of Zymar and Vigamox has only been demonstrated compared with placebo. A randomized, double-blind trial of 100 patients demonstrated...
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**TABLE**

Commonly used ophthalmic antibiotics

<table>
<thead>
<tr>
<th>Antibacterial agent</th>
<th>Trade name</th>
<th>Cost*</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>First-line agents</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Polymyxin B/trimethoprim</td>
<td>Polytrim</td>
<td>$13.99</td>
<td>Available as solution and ointment</td>
</tr>
<tr>
<td>Bacitracin/polymyxin B</td>
<td>Polysporin, AK-Poly</td>
<td>$9.89</td>
<td>Ointment only</td>
</tr>
<tr>
<td>Sodium sulfacetamide</td>
<td>Sulf-10, Bleph-10, Sulamyd, Isopto-Cetamide, AK-Sulf</td>
<td>$7.99</td>
<td><em>S. aureus</em> resistance increasing, available as solution and ointment</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>Ilotycin, AK-Mycin</td>
<td>$11.99</td>
<td>Ointment only</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>AK-Tracin</td>
<td>$7.99</td>
<td>Ointment only</td>
</tr>
<tr>
<td><strong>Alternatives</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neomycin/polymyxin B/bacitracin</td>
<td>Neosporin</td>
<td>$7.99</td>
<td>High rate of allergic reaction to neomycin, ointment only</td>
</tr>
<tr>
<td>Aminoglycosides</td>
<td>Genoptic, Tobrex</td>
<td>$8.99–$15.99</td>
<td>Corneal damage with prolonged use, available as solution and ointment</td>
</tr>
<tr>
<td>Older fluoroquinolones</td>
<td>Ciloxan, Iquix, Quixin, Ocuflox</td>
<td>$29.99–$56.99</td>
<td>Significant concern for class resistance, solution only</td>
</tr>
<tr>
<td>Fourth-generation fluoroquinolones</td>
<td>Vigamox, Zymar</td>
<td>$69.99–$74.06</td>
<td>Expensive, concern for emerging resistance, solution only</td>
</tr>
<tr>
<td>Azithromycin</td>
<td>AzaSite</td>
<td>$64.99</td>
<td>Less frequent dosing, expensive, concern for emerging resistance, solution only</td>
</tr>
</tbody>
</table>


the superiority of 5 days of Zymar over placebo in terms of clinical (77% vs 58%, *P*=.05) and microbiologic (92 vs 72%, *P*=.009) cures. Similarly, in an unpublished study, 4 days of Vigamox produced clinical and microbiologic cures in 66% to 69% (*P*<.05) and 84% to 94% (*P*<.05) of patients, respectively. Compared with placebo, AzaSite for 5 days produced clinical and microbiologic cure in significantly more patients (63% vs 50%, *P*=.03 and 88% vs 66%, *P*=.001, respectively). In a trial of 1,043 patients with bacterial conjunctivitis, the efficacy of AzaSite was shown to be similar to that of tobramycin (88% vs 89% with clinical cure), but was quicker to resolve symptoms.

Adverse events, most frequently transient burning and stinging that were generally mild and usually resolved spontaneously without treatment, occurred in few patients (ie, 5%–10%) treated with Zymar, Vigamox, or AzaSite in these clinical trials.

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Is biofeedback an effective treatment for essential hypertension?

Summary
Biofeedback lowers blood pressure in adults with mild hypertension, and may be most effective when combined with other relaxation techniques. (SOR B, based on a systematic review and randomized controlled trial). Most studies have included patients also receiving antihypertensive medications, but limited evidence indicates that the response to biofeedback is similar in unmediated groups.

The Evidence
Approximately 27% of adults aged 25 and older have hypertension. Only about 34% of this population has their blood pressure (BP) under control. Low adherence to antihypertensive medications is often responsible for poor BP control. Biofeedback, which involves the use of electronic instruments to measure and provide auditory or visual feedback to patients about their neuromuscular and autonomic nervous system activity, has been used as a nonpharmacologic treatment of hypertension.

Biofeedback lowers BP
A systematic review of randomized control trials examined biofeedback as a treatment for adults with essential hypertension. Hypertension was defined as a systolic blood pressure (SBP) ≥140 mmHg and/or a diastolic blood pressure (DBP) ≥90 mmHg. Twenty-two studies with a total of 471 patients in the biofeedback group and 434 patients in the control group were included in the review, and the average pretreatment BP was 145/93 mmHg. In most studies the patients were also taking antihypertensive medications.

The 22 studies yielded average treatment effects of biofeedback of −5.5 mmHg for SBP and −4.4 mmHg for DBP. Negative values indicated the biofeedback group had a larger decrease in BP than did the control group.

Other relaxation techniques enhance the BP-lowering effect
The authors further examined the effect of biofeedback compared with either a no-intervention control group or a sham intervention control group. Fourteen studies compared biofeedback, with or without other relaxation techniques, with a control group receiving no interventions. Significant treatment effects were found for biofeedback on both SBP (−7.3 mmHg) and DBP (−5.8 mmHg). Treatment effects in the 5 studies with no antihypertensive drugs were −9.5 mmHg systolic and −7.4 mmHg diastolic.

Patients who received biofeedback treatment alone had significantly lower DBP only, when compared with the controls, whereas patients who received biofeedback and relaxation treatment had significantly lower SBP and DBP. Biofeedback decreased SBP and DBP more than no intervention (P < .001), but not more than sham intervention (P > .05). Biofeedback was found to be superior to sham intervention only when it was combined with other relaxation techniques. No differences were noted based on the type of feedback used (blood pressure, skin temperature, etc).

Biofeedback better than sham intervention
In a recent randomized controlled trial not included in the review, 42 adults diagnosed with mild hypertension and who had not been on any cardiovascular or antihypertensive medication during the previous 2 months, were assigned to active biofeedback or a sham biofeedback control group. All participants were monitored during a 2-week run-in period during which BP was measured weekly. The groups were comparable in demographics, lifestyle variables, and anxiety levels, but the baseline BP was significantly higher in the treatment group. Both groups were taught diaphragmatic breathing.

The biofeedback group received 4 weekly 40- to 45-minute training sessions in which they were instructed in sets of lowering their SBP with 3 minutes of diaphragmatic breathing, resting for 1 minute, and then raising SBP with 1 minute of mental activity. They received feedback of their progress by watching a display of their beat-to-beat BP signals measured with a finger arterial pressure device. The sham group received 4 weekly sessions of instruction in the same sets of diaphragmatic breathing and mental activity, but without any feedback. The groups were advised to practice
diaphragmatic breathing twice daily, without any biofeedback available to them, during the 8-week follow-up period. They were also asked to self-monitor their BP, but the study did not provide details as to how the participants accomplished this.

The biofeedback group achieved a significantly greater decrease in mean SBP from baseline to 12-week follow-up (148.4 mmHg at baseline to 135.7 mmHg at follow-up) than did the sham group (142.1 to 138.1 mmHg, \( P = .013 \) for comparison of the changes). Mean arterial pressure (MAP) levels were also lower significantly lower in the biofeedback group (112.6 mmHg at baseline to 104.4 mmHg at follow-up) versus the sham group (110.1 to 106.8 mmHg, \( P = .026 \) for comparison of the changes).

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REFERENCES
1. The dietary supplement red yeast rice has been:
   - a. Opposed by the US Food and Drug Administration
   - b. Shown to vary widely across brands for monacolin content
   - c. Reported in case studies to cause symptomatic myopathy
   - d. All of the above

2. Which group recommends discontinuing osteoporosis screening in low-risk women older than 80 years?
   - a. US Preventive Services Task Force
   - b. National Osteoporosis Foundation
   - c. American Geriatric Society
   - d. None of the above

3. High-trauma fractures in adults older than 65 years
   - a. Are not associated with osteoporosis
   - b. Most often result in wrist and rib injuries
   - c. May be caused by a fall from a standing height
   - d. Are unambiguously defined by the stress forces applied to bone

4. A 45-year-old man with a body mass index of 30 is newly diagnosed with type 2 diabetes. All of his laboratory findings are within normal limits, except his blood glucose is 212 mg/dL and his hemoglobin A1c is 9%. What is the best initial treatment for his diabetes?
   - a. Metformin
   - b. Pioglitazone
   - c. Glargine insulin
   - d. Glipizide

5. Which of the following treatments has consistent recommendations for patients with renal failure or heart failure and diuretic-resistant volume overload?
   - a. Bolus administration of loop diuretics
   - b. Continuous infusion of thiazide diuretics
   - c. Combining loop diuretics with thiazide-type diuretics
   - d. Sodium and fluid restriction

6. Which in-office treatment for molluscum contagiosum is the most effective?
   - a. Watchful waiting
   - b. Imiquimod
   - c. Cantharidin
   - d. Curettage

7. Which of the following conditions is the most common cause of delayed menarche in a girl without secondary sexual characteristics?
   - a. Constitutional delay
   - b. Hypogonadotropic hypogonadism
   - c. Prolactinoma
   - d. Uterine agenesis

8. Which of the following ophthalmic antibiotics is the best first-line treatment for acute bacterial conjunctivitis?
   - a. Zymar
   - b. Vigamox
   - c. Polytrim
   - d. AzaSite

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Arthritis and Exercise

Getting up, moving, and stretching may seem like the last thing you want to do when your joints ache. Osteoarthritis can affect any joint, causing stiffness and pain with walking, bending over, and doing everyday activities with your hands. Over time, joints may be damaged from arthritis, and an ongoing lack of exercise weakens the muscles that could otherwise help support the joints. Medications can help to relieve pain, but they do not help strengthen these areas around the joints.

General benefits of exercise
Exercise helps maintain a healthy mind and body for everyone. Moderate exercise helps increase energy and stamina, and helps with fatigue and sleeping problems. Exercise also helps relieve anxiety and mild depression and is an important part of maintaining a healthy weight and a healthy heart.

What do the latest studies show about exercise and arthritis?
Regular exercise has actually been shown to provide moderate relief of arthritis pain. We also know that sensible exercise, started slowly and increased gradually with periods of rest, does not harm arthritic joints. More studies are needed to determine if exercise can also relieve the stiffness that is part of arthritis symptoms.

The right kind of exercise can strengthen the muscles around diseased joints, reducing the risk of injury. (The best kinds of exercises move the whole body, not just the affected joints.) Exercise also increases the fluid that helps lubricate the joints to keep them flexible.

Regular physical activity also helps to achieve a normal weight. Excess weight contributes to stress on the joints, especially knees and hips. Losing even a few pounds can really help to make you feel better.

Take action
Your doctor can get you started in the right direction. Doctors can recommend physical therapy to show you the best way to increase range of motion and strength. The Arthritis Foundation encourages the PACE program (People with Arthritis Can Exercise) and warm water exercise programs. Tai chi and some types of yoga are also recommended. You can help to protect affected joints by avoiding too much repetitive movement and rapid or jarring movements, and by not increasing a new exercise too quickly.

Gradually increase everyday activities, like walking, and make exercise part of your lifestyle. Your joints will be glad you did.

For more information
Fitness (Arthritis Today, published by the Arthritis Foundation)
http://www.arthritis.org/fitness.php

Osteoarthritis (American College of Rheumatology)

Osteoarthritis (MedlinePlus)