We might better serve our patients by improving our examination skills than by urging self-exams. We should inform women who choose to practice breast self-examination that they run a higher risk of having a breast biopsy that does not reveal a cancer and that it is not known whether self-examination reduces a woman's chance of dying from breast cancer. Mammography is neither perfectly sensitive nor universally available, and many women detect breast cancer themselves; it remains important for women to know how their breasts look and feel in order to recognize and report any anomalies. But we might better serve our patients by improving our clinical breast examination skills than by urging them to perform regular self-exams; clinicians who spend 3 minutes per breast and use proper technique (vertical strip search pattern, thoroughness, varying palpation pressure, 3 fingers, circular motion, finger pads) have significantly better sensitivity and specificity than those who do not.

Breast self-examination has little or no impact on breast cancer mortality and cannot be recommended for cancer screening (strength of recommendation [SOR]: A, based on a systematic review of high-quality randomized, controlled trials [RCTs]). Clinical breast examination is an important means of averting some deaths from breast cancer, but demands careful attention to technique and thoroughness (SOR: B, extrapolating from a high-quality RCT).

**Evidence summary**

Breast cancer is the second leading cause of cancer death among American women; 1 in 8 women will be diagnosed with breast cancer in her lifetime, and 1 in 30 will die of it. Breast cancer screening and mammography have become almost synonymous. But physical examinations by clinicians or women themselves remain important methods of screening to consider.

Breast self-examination is appealing as a patient-centered, inexpensive, non-invasive procedure that empowers women and is universally available. However, a recent Cochrane review found no evidence of benefit from self-screening.

Two large RCTs, conducted in St Petersburg, Russia (122,471 women) and Shanghai, China (266,064 women), were found. Both studies used cluster randomization (by worksite) and involved large numbers of women who were meticulously trained in proper breast examinations.
self-examination technique and had numerous reinforcement sessions. Study compliance and follow-up were excellent. Outcomes assessment was explicitly blinded in the Shanghai study. Neither trial demonstrated a reduction in breast cancer mortality or improvement in the number or stage of cancers detected during 9 to 11 years of follow-up, but there is evidence for harm: a nearly 2-fold increase in false-positive results, physician visits, and biopsies for benign disease.4

No trials comparing screening clinical breast examinations alone to no screening have been reported, but good indirect evidence of efficacy comes from the results of the Canadian National Breast Screening Study-2 (CNBSS-2). A total of 39,405 women aged 50 to 59 years were randomized to screening with clinical exams plus mammography or clinical exams alone. Other large RCTs have shown a consistent benefit to mammography screening for women of this age (in-depth independent reviews of recent criticism of the trials have concluded that their flaws do not negate mammography’s efficacy in reducing breast cancer mortality).3,6 The CNBSS-2 trial showed no mortality advantage when mammography was added to an annual, standardized 10- to 15-minute breast examination, implying that careful, detailed, annual clinical breast examinations may be as effective as a mammography screening program.3

Recommendations from others
The US Preventive Services Task Force found insufficient evidence to recommend for or against routine clinical exams alone to screen for breast cancer, or to recommend for or against teaching or performing routine breast self-examination.7 The Canadian Task Force on Preventive Health Services recommends against teaching self-examination to women aged 40 to 69 years due to “fair evidence of no benefit and good evidence of harm.”7,8

The American Cancer Society continues to recommend periodic clinical exams,4 and women who choose to do self-examination should receive instruction and have their technique reviewed during periodic health examinations; it is acceptable for women to choose not to do self-examinations. The American Academy of Family Physicians concludes that the evidence is insufficient to recommend for or against breast self-examination.9 The American College of Obstetricians and Gynecologists recommends both.10

REFERENCES
What are the relative risks and benefits of progestin-only contraceptives?

Mary W. Roederer, PharmD
Department of Family Medicine, University of North Carolina at Chapel Hill

Jean C. Blackwell, MLS
Health Sciences Library, University of North Carolina at Chapel Hill

**EVIDENCE-BASED ANSWER**

Little evidence describes the risks and benefits of progestin-only contraceptives therapy options.

**Risks**

No good-quality evidence exists to determine the risk of cancer associated with progestin-only contraceptives. Data are insufficient to discern their effect on milk quality and quantity during lactation, though no effect on infant growth or weight was identified (strength of recommendation [SOR]: A, based on systematic Cochrane review).1

No increase in blood pressure occurred with oral progestin-only contraceptives or depot medroxyprogesterone acetate (DMPA) (SOR: B, cohort studies).2 A decrease in bone mineral density was associated with current use of DMPA in studies lasting 2 years or less, yet the cessation of use may attenuate the effect (SOR: B, mostly case-control).3 Oral and injectable progestin-only contraceptives demonstrated no significant increase in venous thromboembolism, stroke, acute myocardial infarction, or combined cardiovascular disease endpoint (SOR: B, case-control study).4 Termination rates for nonmenstrual effects with progesterone implants were less than 3% (SOR: B, cohort studies).5

**Benefits**

Progestin-only contraceptives are an effective form of birth control. For the treatment of premenstrual syndrome or dysfunctional uterine bleeding, inadequate evidence exists to support using progestin-only options (SOR: A, RCTs).6,7

**Evidence summary**

The risks and benefits associated with progestin-only contraceptives are not completely studied for all routes of administration. There is insufficient evidence regarding their risks to point to a definitive harm with their administration (TABLE).

The risk of pregnancy with progestin-only contraceptives ranges from 0.0% to 13.2% based on the method that is selected.8 Evidence is lacking to support use of progestin-only contraceptives for premenstrual syndrome or dysfunctional uterine bleeding.6,7

**CLINICAL COMMENTARY**

Patient-centered, not evidence-based, reasons contribute to shifts in contraception patterns

Nonlactating women in my practice are choosing progestin-only contraceptives less often than previously, when DMPA was my second-most-common contraceptive prescription. Patient-centered, not evidence-based, reasons contribute to this shift in prescribing patterns.

Many women who chose injectable progestin-only contraceptives because of difficulty remembering to take oral contraceptives have changed to patch-delivered or intravaginal estrogen-progestins due to concern over potential weight gain and increased bone loss with progestin-only contraceptives. Intrauterine devices have experienced a surge in popularity with the addition of slow-release progesterone, and condoms remain popular because they reduce disease transmission. When women receive evidence-based risk/benefit contraceptive counseling, they then have the knowledge to choose the contraceptive that best fits their lifestyle.

Paul Crawford, MD, Headquarters AAC Family Medicine Residency, Eglin Air Force Base, Eglin, Fla
**TABLE**

<table>
<thead>
<tr>
<th>RISK</th>
<th>TYPE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>VTE, stroke, acute MI, or combined CVD endpoint</td>
<td>Oral injectable</td>
<td>No significant association with increased incidence of VTE, stroke, acute MI, or the combined CVD endpoint</td>
</tr>
<tr>
<td>Increased blood pressure</td>
<td>Oral DMPA</td>
<td>No significant association with increased blood pressure for up to 2–3 years of use</td>
</tr>
</tbody>
</table>
| Nonmenstrual adverse events | Progesterone implants | • Specific information for each adverse event unavailable  
• Overall termination rate for nonmenstrual adverse events less than 3% |
| Effect on lactation | All progestin-only contraceptives* | • Insufficient evidence to establish an effect on milk quality or quantity  
• No documented effect on infant growth or weight |
| Decreased BMD | DMPA | • Decreased bone mineral density within 1 standard deviation of mean  
• Duration of effect inconclusive as cessation of use may attenuate effect  
• No information on risk of fracture |
| Pregnancy | Oral, DMPA, progesterone implants | Based on perfect use and typical use evaluations:  
• Oral: 0.0% to 13.2%  
• DMPA: 0.0% to 3.2%  
• Implants: 0.0% to 2.3% |

**BENEFIT**

<table>
<thead>
<tr>
<th>TYPE</th>
<th>EVIDENCE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of PMS</td>
<td>Suppositories, pessaries, oral</td>
</tr>
<tr>
<td>Dysfunctional uterine bleeding with anovulation</td>
<td>Oral</td>
</tr>
</tbody>
</table>

---

**Recommendations from others**

The World Health Organization (WHO) highlights the need to avoid progestin-only contraceptives for women younger than 18 or older than 45 years, secondary to concerns of decreased bone mass. Immediately postpartum, women may initiate progestin-only contraceptives if they are not breastfeeding; if breastfeeding, women should wait until at least 6 months postpartum.

Hypertensive women should avoid progestin-only contraceptives; women at risk for hypertension—particularly DMPA users—are encouraged to measure blood pressure before and after use. The WHO document points out the increased possibility for abnormal uterine bleeding with progestin-only contraceptives use.9

American College of Physician’s PIER: Physicians’ Information and Education Resource describes using progestin-only contraceptives in hypercoagulable states and severe hyperlipidemia and avoiding use in osteoporosis, osteopenia, and chronic glucocorticoid use due to a decrease in bone mineral density.10
The American College of Obstetricians and Gynecologists (ACOG) specifically endorses the preferential use of progestin-only contraceptives by lactating women and women at an increased risk of venous thromboembolism based on good evidence. For women with systemic lupus erythematosus, ACOG recommends use of progestin-only contraceptives over combined oral contraceptives, based on fair evidence. By consensus, ACOG recognizes benefits of DMPA for women with sickle-cell disease and women with coronary artery disease, congestive heart failure, or cerebrovascular disease. In general, ACOG recommends progestin-only contraceptives over combined oral contraceptives for patients with the following conditions: migraine headaches, cigarette smoker of age greater than 35, history of venous thromboembolism, coronary artery disease, congestive heart failure, cerebrovascular disease, postpartum <2 weeks, hypertension with vascular disease or age greater than 35, diabetes with vascular disease or age greater than 35, systemic lupus erythematosus with vascular disease, nephritis, or antiphospholipid antibodies, or hypertriglyceridemia.11

REFERENCES
What is the initial work-up in the diagnosis of hypertension?

Brett V. Daniel, MD, Gary Kelsberg, MD
Valley Family Medicine Residency, Renton, Wash

Terry Ann Jankowski, MLS
University of Washington, Seattle

**Evidence-based answer**

Patients with a new diagnosis of hypertension should be evaluated with a history and physical exam and the following initial studies: serum potassium and creatinine, fasting serum glucose and lipid panel, hematocrit, urinalysis, and electrocardiogram (strength of recommendation [SOR]: C, based on a consensus of expert opinion). Consensus is lacking for measuring serum sodium, calcium, and uric acid.

Testing for microalbuminuria is optional in the work-up for a patient without diabetes (SOR: C, expert consensus). Some expert panels list limited echocardiography as another option.

**Clinical commentary**

Not all recommendations for working-up hypertensive patients are cost-effective

There is obvious enthusiasm among the expert panels for a detailed workup of patients with hypertension. But are the recommendations cost-effective? Annual urine dipstick testing beginning at age 30 for hypertensive patients is highly cost-effective. Identification of proteinuria and treatment with an ACE inhibitor or angiotensin receptor blocker prevents the progression of renal disease at a quality-adjusted life-year cost of $15,484 to $26,320, depending on the age group.1 Unfortunately, evaluation for secondary causes of hypertension, screening for LVH, and ruling out comorbidities have not been explicitly evaluated for cost-effectiveness.

**Evidence summary**

There are currently no large outcome studies evaluating the initial work-up of hypertension; however, 4 international expert panels have published recommendations.2-5 These panels advise 3 initial objectives: 1) assess lifestyle and identify other cardiovascular risk factors or concomitant disorders that may affect prognosis and guide treatment; 2) search for treatable causes of high blood pressure; and 3) assess for the presence of target organ damage that would change the management of the patient (such as chronic kidney disease or heart disease).

In addition to a thorough history and physical, the following studies are recommended for patients with newly diagnosed hypertension:

- **Serum potassium and creatinine.** All 4 panels recommend measuring serum potassium and creatinine in order to: 1) monitor the effects of diuretics and angiotensin-converting enzyme (ACE) inhibitors used in hypertension therapy, 2) screen for unexplained hypokalemia that may indicate a low-renin form of hypertension, 3) calculate baseline creatinine clearance, and 4) screen for chronic kidney disease.

- **Fasting blood glucose.** All 4 panels recommend measuring a fasting glucose level to screen for diabetes. An abnormal glucose level may also reveal glucose intolerance, one of the diagnostic criteria of metabolic syndrome. Up to 60% of patients with diabetes also have hypertension.6

- **Fasting lipid panel.** All 4 expert panels
recommend screening for dyslipidemia with a fasting lipid panel to assess cardiovascular risk. A cohort study evaluating 336,222 men aged 35 to 57 years found a continuous, positive, graded correlation between plasma cholesterol levels and coronary risk.7

**Hematocrit.** All 4 panels recommend a hematocrit to screen for anemia, which may be due to chronic kidney disease.

**Urinalysis.** All 4 panels recommend a urinalysis to screen for renal disease.

**Electrocardiogram (ECG).** All 4 panels recommend an ECG to screen for findings associated with hypertension, including left ventricular hypertrophy (LVH), myocardial infarction, and rhythm abnormalities. A cohort study followed 2363 patients for 14 years who had untreated hypertension and were without pre-existing cardiovascular disease. After controlling for age, sex, diabetes, and mean blood pressure, LVH by ECG conferred a significant increased risk for cerebrovascular events (relative risk=1.79; 95% confidence interval [CI], 1.17–2.76). However, in a cohort of 4684 subjects from the Framingham Heart Study, ECG had a sensitivity of only 6.9% for the detection of LVH (specificity 98.8%; positive likelihood ratio=5.3; negative likelihood ratio=0.94).8

**Echocardiography.** Two panels3,4 and an online text10 recommend echocardiography, preferably limited echo, as an optional study. A systematic review of studies comparing the sensitivities and specificities of ECG and echo found that each was highly specific for the detection of LVH (77%–97%), but the sensitivity of echocardiography (88%–93%) exceeded that of ECG (21%–54%). However, LVH detected by ECG is a better predictor of cardiovascular complications.11 Because echocardiography may help assess disease duration and guide management, both panels recommend it for patients with severe or refractory hypertension but without other target organ damage.

**Microalbuminuria.** All panels listed microalbuminuria testing as an optional study for patients without diabetes because of its association with an increased incidence of cerebrovascular disease.12 It is unclear whether microalbuminuria results from the increased intraglomerular pressure in hypertension or if it represents glomerular damage.13

**Sodium, calcium, uric acid.** There is no consensus on the routine inclusion of several studies: serum sodium (recommended by 2 panels and an online text3,4,10), serum calcium (recommended by 1 panel and the text10), and uric acid (1 panel recommends it while the text10 lists it as optional).

**Recommendations from others**

Recommendations from major organizations are included in Evidence Summary, above.

**REFERENCES**


11. Dijkstra RF, van Schayck CP, Bakx JC, Thien T, Verheugt FW, Mokkink HG. Left ventricular hypertrophy: differences in the diagnostic and prognostic value of elec-


**ACKNOWLEDGMENTS**

The opinions and assertions contained herein are the private views of the author and are not to be construed as official, or as reflecting the views of the US Air Force Medical Service or the US Air Force at large.

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**Clinical Inquiries**

Clinical Inquiries answer recent questions from the practices of family physicians. Practicing family physicians choose the most relevant questions submitted through a web-based voting system operated by the Family Physicians Inquiries Network (FPIN; online at www.fpin.org).

FPIN is national, not-for-profit consortium of family medicine departments, community residency programs, academic health sciences libraries, primary care practice-based research networks, and other specialists. Once questions are selected, FPIN editors then organize teams of clinicians and librarians to answer them based on systematic review of the world literature. Answers are developed through an explicit, systematic method:

1. FPIN librarians and editors identify questions recently answered in best evidence sources (e.g., Cochrane Reviews, Clinical Evidence, the US Preventive Services Task Force, Evidence Based Guidelines, a published systematic review).

2. FPIN librarians then conduct systematic and standardized literature searches of best evidence sources, Medline, and other databases in collaboration with an FPIN clinician or clinicians. If a best evidence source has been identified, the search begins from the date of the search conducted for that source. Otherwise, the searches are comprehensive.

3. FPIN clinician authors then choose the highest quality original research sources, and critically appraise the research and integrate the findings in the Evidence Based Answer and Evidence Summary section of Clinical Inquiries. Authoritative sources are also quoted in the “Recommendations from Others” section of the Clinical Inquiry.

4. Each Clinical Inquiry is reviewed by 4 or more peers or editors before publication in *JFP*.

5. FPIN medical librarians are accountable for the thoroughness of the literature search, for recording the databases searched, search hedges used and the search terms. The details of each search is available to any interested reader (contact managingeditor@fpin.org).

6. Finally, a practicing family physician or other clinician writes an accompanying commentary to provide a clinical perspective.
Does early detection of suspected atherosclerotic renovascular hypertension change outcomes?

Sandra Shepherd, MD, Kara Cadwallader, MD
Family Practice Residency of Idaho, Boise

Terry Ann Jankowski, MLS
University of Washington Health Science Library, Seattle

**Evidence-based answer**

We found no evidence for changed outcomes from early detection of renal artery stenosis (RAS). Treatment of RAS in refractory hypertension modestly improves blood pressure control. There was a trend toward improved clinical outcomes but studies were underpowered to demonstrate this (strength of recommendation [SOR]: A, based on systematic review of RCTs).

Treatment of RAS in chronic renal impairment does not appear to improve renal function nor change clinical outcomes, but data are conflicting (SOR: A, based on 2 RCTs and multiple cohort studies). Subgroups of patients who have recurrent episodes of congestive heart failure or flash pulmonary edema exhibit functional improvement following percutaneous transluminal renal angioplasty (PTRA) with stent placement. (SOR: C, based on a retrospective cohort study).

Computed tomography (CT) angiography and magnetic resonance angiography (MRA) are the most accurate and cost-effective noninterventional diagnostic modalities for RAS (SOR: A, based on a large meta-analysis).

While revascularization effectively improves patency, the complication rate is high and deaths have occurred (SOR: B, based on randomized controlled trials [RCTs]). Patients with worse renal function tend to do more poorly (SOR: C, based on retrospective cohort studies). Data are insufficient to recommend a method of revascularization (surgical vs PTRA with or without stenting) (SOR: C, based on multiple cohort studies).

**Clinical commentary**

When herding hypertensives, treat them all like horses, not zebras

“When you hear hoofbeats, think of horses. You will occasionally see a zebra and very rarely a unicorn.” Patients who benefit from physicians looking for and treating renovascular hypertension are unicorns, not zebras. A very few patients benefit by needing fewer drugs, while a few are harmed by complications of revascularization. No benefit in overall mortality, disease specific mortality or vascular morbidity (stroke, heart disease) has been demonstrated. So, the take-home message is: When herding hypertensives, treat them all like horses—you may stumble across a few zebras, but looking for benefit from discovering and treating renovascular hypertension is as fruitful as looking for unicorns—a product of imagination, myth, and hope, not based in reality. Based on this Clinical Inquiry, I will stop feeling guilty about not searching diligently for renovascular causes of “curable hypertension.”

Dan Triezenberg, MD
Family Practice Residency, Saint Joseph Regional Medical Center, South Bend, Ind

**Clinical inquiries**

“Early” diagnosis of renovascular hypertension is best defined as diagnosis while blood pressure is controlled by medications or when renal function remains normal.

Hypertension. A meta-analysis (3 RCTs, total n=210 patients) examining balloon angioplasty for RAS and poorly controlled hypertension showed modest but significant effect on blood pressure control. Comparing the angioplasty group with medical management, the mean reduction...
Only patients with CHF or flash pulmonary edema clearly benefit from stenting.

in blood pressure was –7 mm Hg systolic (95% confidence interval [CI], −12 to −1) and −3 mm Hg diastolic (95% CI, −6 to −1). Patients treated with balloon angioplasty were more likely to use fewer antihypertensive medications (unable to synthesize data for quantity) and to have fewer major cardiovascular and renovascular complications (not defined specifically) (odds ratio [OR]=0.27; 95% CI, 0.06–1.23; _P_=.09).¹ One cohort study of 150 patients found that stenting bilateral (vs unilateral) RAS predicted a more beneficial blood pressure response (OR=4.6; _P_=.009).²

Renal impairment. The value of RAS intervention for patients with hypertension and worsening renal function is unclear. One RCT of 106 patients with atherosclerotic RAS and serum creatinine (Cr) of <2.3 mg/dL compared PTRA with medical therapy of hypertension. By an intention-to-treat analysis, there was no significant difference in renal function at 12 months between the groups.³ A nonblinded RCT of 85 patients found no change in mortality or renal function with intervention. Three groups were compared: observation of 52 patients with unilateral RAS (>50%), intervention on 12 patients with bilateral RAS, and observation of 21 patients with bilateral RAS. All groups reported 32% mortality at 2 years. Only 3 of the 27 deaths were directly related to renal disease (2 from the observation group with unilateral RAS and one from the intervention group).⁴ Cohort studies, using different measures of renal function, report improvement, stabilization, or worsening following intervention.¹⁻⁷

Congestive heart failure and flash pulmonary edema. Patients who have recurrent episodes of congestive heart failure or flash pulmonary edema with severe RAS have marked functional improvement following PTRA with stenting. One retrospective cohort study (n=39) reported a decrease in hospitalizations (from 2.4 ± 1.4 per year to 0.3 ± 0.7 per year; _P_<.001) and improvement in New York Heart Association heart failure functional classification (2.9 ± 0.9 to 1.6 ± 0.9).⁸

Diagnosis. MRA (sensitivity 99%, specificity 93%) and CT angiography (sensitivity 97%, specificity 95%) are the most accurate and cost-effective, based on a large meta-analysis.⁹

Complications. Serious or potentially serious complications (ie, bleeding, renal artery injury, need for hemodialysis) were seen in 13% to 25% of patients who underwent angioplasty.²⁻⁷ Combining 3 studies (n=632), there were 5 procedure-related deaths.⁵⁻¹⁰ Worsened patient survival correlated with Cr >1.7 mg/dL or age >70 (OR=9.96, _P_<.0001 and OR=3.4, _P_=.001, respectively). Worsened renal survival was present in the same subgroups (OR=7.8, _P_<.001 and OR=2.7, _P_ <.01, respectively).⁷

Recommendations from others

The American Heart Association lists 3 clinical criteria for revascularization: 1) hypertension (accelerated, refractory, or malignant), 2) renal salvage, 3) cardiac disturbance syndromes (recurrent “flash” pulmonary edema or unstable angina with significant RAS).¹¹ JNC 7 does not recommend looking for RAS unless hypertension is uncontrollable.¹²

The Society of Nuclear Medicine recommends that only moderate- to high-risk individuals be screened for RAS. This guideline clarifies that RAS does not equal renovascular hypertension and that the future “gold standard” diagnosis of renovascular hypertension should be the response to successful revascularization.¹³

References


CONTINUED ON PAGE 816
Is yearly chest x-ray screening helpful in reducing mortality for smokers?

Kimdary Chek, MD, MPH, Joseph Tribuna, MD
Overlook Family Practice Residency, Summit, New Jersey
Joan Nashelsky, MLS
Family Practice Inquiries Network, Iowa City, Iowa

**EVIDENCE-BASED ANSWER**

For current and former smokers, the evidence does not support yearly chest x-rays to decrease lung cancer mortality (strength of recommendation [SOR]: A, based on multiple randomized controlled trials). Even with the addition of sputum cytology and more frequent chest x-rays, lung cancer mortality was unchanged (SOR: A).

**CLINICAL COMMENTARY**

Reduce morbidity and mortality by helping patients quit smoking

The bottom line is that morbidity and mortality are not reduced when we use chest x-rays, sputum cytology, or a combination of the 2 in screening for lung cancer. One thing we can do for our patients is counsel them about the ill effects of tobacco use and support them in their smoking cessation efforts. Although there is no guarantee that those who quit will not get lung cancer, cessation certainly reduces the risk and brings other health and financial benefits.

Of interest is the ongoing National Lung Screening trial, which compares screening spiral CT scans with chest x-rays in the detection of lung cancer. This large trial, sponsored by the NCI, will compare both modalities over 8 years and should help determine if either test is better at reducing morbidity and mortality from this disease.

Evidence summary

Five randomized controlled trials have examined lung cancer mortality after screening chest x-rays. In the first trial—the only one that included former as well as current smokers and nonsmokers—subjects were randomized to undergo chest x-ray studies every 6 months, or at baseline and again at the end of the 3-year study. After 3 years, there was no statistically significant mortality difference with more frequent chest x-rays.1,2

Another trial involved male smokers who were randomized to undergo chest x-ray and sputum cytology either every 6 months or after 3 years. After 3 years, both groups were screened annually with chest x-ray alone for an additional 3 years. There was no significant difference in lung cancer mortality at any point, including at a 15-year post-trial follow-up.3 Both studies showed earlier detection and longer survivorship of lung cancer among screened vs nonscreened groups due to lead-time bias (because the cancer was detected earlier from screening vs clinical diagnosis, it falsely appears to prolong survival). Overall mortality was the same in both groups.

The National Cancer Institute (NCI) sponsored 3 randomized controlled trials on lung cancer screening for male smokers involving 3 major medical centers. The studies were designed to determine the incremental benefit of adding sputum cytology to chest x-ray screening. In 2 of the NCI studies, participants were randomly assigned to receive annual chest x-ray only or a dual screen with annual chest x-ray and sputum cytologies every 4 months. In both studies, there was no statistical difference in lung cancer mortality between the 2 groups.4-6 The third NCI study randomized participants to chest...
of lung cancer symptoms those without chest x-rays for against serial AAFP, and ACCP Cancer Society, The American FAST 816 VOL 54, NO 9 / SEPTEMBER 2005

CLINICAL INQUIRIES

x-ray and sputum cytology either every 4 months or annually. Again, there was no significant difference in lung cancer mortality, even after an extended follow-up of 20.5 years. Adding sputum cytology to chest x-ray only improved lung cancer detection rates over chest x-ray alone.

A significant limitation of the 5 studies presented is that no true control or non-screening groups determined the real efficacy of screening chest x-rays vs no screening. The goal of a study of a screening program is to detect a disease early enough so that treatment can alter mortality. These uncontrolled studies of routine screening chest x-rays, no matter how frequently performed, do not meet this criteria for current and former smokers.

Recommendations from others
The US Preventive Services Task Force does not recommend for or against screening asymptomatic or high-risk persons for lung cancer with either low-dose computed tomography (CT), chest x-ray, sputum cytology, or a combination of these tests. The American Cancer Society and American Academy of Family Physicians recommend against the use of chest x-ray or sputum cytology in asymptomatic high-risk persons. The American College of Chest Physicians recommends against the use of serial chest x-rays for individuals without symptoms or without a history of cancer. They do not comment about high-risk groups—that is, current or former smokers.

REFERENCES

FAST TRACK
The American Cancer Society, AAFP, and ACCP all recommend against serial chest x-rays for those without symptoms of lung cancer

CONTINUED FROM PAGE 814

What is the diagnostic approach to a patient with leg cramps?

Hayam K. Shaker, MD
Hendersonville Family Practice Residency Program, MAHEC, Hendersonville, NC
Leslie Mackler, MLS
Moses Cone Health System, Greensboro, NC

Leg cramps are very common (strength of recommendation [SOR]: C, case series), and most cases have no detectable cause (SOR: C, expert opinion). Arterial vascular disease and neurological diseases are more prevalent among male patients with leg cramps (SOR: C, small case series).

History and physical should focus on detecting precipitating factors for iron deficiency anemia (gastrointestinal bleeding, frequent blood donations, menorrhagia), electrolyte imbalance (renal disease, fluid losses), endocrine disorders (thyroid, Addison’s disease), neuromuscular disorders (neuropathies and myopathies), and medication use (antidepressants and diuretics). Laboratory testing is guided by the history and physical and may include ferritin, electrolytes, blood sugar, magnesium, zinc, creatinine, blood urea nitrogen, liver function test, and thyroid-stimulating hormone (SOR: C, expert opinion and nonsystematic review).

If a thorough search reveals no cause, keep your patient educated
Leg cramps are a common nonspecific complaint that can have a significant impact on quality of life. The literature on the potential causes and treatments of leg cramps is limited to small studies and expert opinion. This leaves the clinician on the spot with their own knowledge of medicine and their relationship with the patient. A careful history and physical may suggest some avenues of inquiry while simultaneously excluding other serious causes. Lab and radiology testing can be useful when used in a thoughtful manner. A confusing clinical picture has frustrated me when I was too aggressive with studies. If a thorough search reveals no specific cause, I attempt to keep my patient educated regarding possible complications while keeping my differential diagnosis broad when addressing this problem in future visits.

Evidence summary
More than two thirds of people aged >50 years have experienced leg cramps.¹ Though leg cramps are common, little is known about their actual causation.²,³

A small, retrospective chart review, limited to male patients, identified an association of vascular and neurologic diseases among patients taking quinine, presumably for leg cramps.² Although commonly idiopathic, leg cramps are sometimes associated with various disorders including endocrine, metabolic, occupational, structural, neuromuscular, vascular, and congenital disorders, as well as toxin- and drug-related causes (TABLE).⁴⁻⁵ All reviews suggest that the best diagnostic approach to leg cramps is a thorough history, and careful physical and neurological examination.¹⁻⁴ The health care provider should clarify the onset and duration of leg cramps, any precipitating activity, and factors that provide relief. A detailed history should focus on precipitating factors for iron deficiency anemia (gastro-intestinal bleeding, frequent blood donations, menorrhagia), a history of renal disease (especially end-stage renal failure) and medication use (antidepressants and diuretics).
TABLE

Possible causes of leg cramps

<table>
<thead>
<tr>
<th>CATEGORY</th>
<th>DISEASES</th>
</tr>
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<tbody>
<tr>
<td>Congenital</td>
<td>McArdle’s disease, “Glycogen storage disease,” autosomal dominant cramping disease</td>
</tr>
<tr>
<td>Endocrine disorder</td>
<td>Thyroid disease, diabetes mellitus, Addison’s disease</td>
</tr>
<tr>
<td>Fluid and electrolyte disorder</td>
<td>Hypocalcemia, hyponatremia, hypomagnesemia, hypokalemia, hyperkalemia, chronic diarrhea, hemodialysis</td>
</tr>
<tr>
<td>Neuromuscular</td>
<td>Nerve root compression, motor neuron disease, mononeuropathies, polyneuropathies, dystonias</td>
</tr>
<tr>
<td>Drugs</td>
<td>Calcium channel blockers (nifedipine), diuretics, phenothiazines, fibrates, selective estrogen receptor modulators, ethanol, morphine withdrawal</td>
</tr>
<tr>
<td>Vascular</td>
<td>Peripheral vascular disease</td>
</tr>
<tr>
<td>Toxins</td>
<td>Lead or strychnine poisoning, spider bites</td>
</tr>
<tr>
<td>Occupational</td>
<td>Focal dystonias (in writers, athletes, miners, and musicians)</td>
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<tr>
<td>Others</td>
<td>Diarrhea, liver cirrhosis, chronic alcoholism, sarcoidosis</td>
</tr>
<tr>
<td>Hematological</td>
<td>Iron deficiency anemia</td>
</tr>
</tbody>
</table>

Modified from Kanaan and Sawaya, Geriatrics 2001.

The physical examination should include a search for obvious physical signs of symptoms noted in the history. Neurological examination can exclude most disorders that simulate leg cramps such as contractures, dystonia, myalgia and peripheral neuropathy.

The choice of laboratory investigations such as ferritin, electrolytes, blood sugar, magnesium, zinc, creatinine, blood urea nitrogen, liver function test, and thyroid function test are largely governed by the findings from the history and physical examination. Though neurophysiological research shows that true muscle cramps are caused by explosive hyperactivity of motor nerves, using diagnostic tools such as electromyography, muscle biopsy, and muscle enzymes are seldom needed.

Because of the lack of well-designed, randomized controlled studies, this diagnostic approach is based on non-systematic reviews, and may differ for individuals based on history and clinical examination.

Recommendations from others
UpToDate states, “a careful history and examination can exclude the majority of disorders in the differential diagnosis” of leg cramps.

REFERENCES