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Best Prescription Strategy for Acute Sore Throat

ABSTRACT & COMMENTARY

By **Rahul Gupta, MD, MPH, FACP**

Clinical Assistant Professor, West Virginia University School of Medicine,
Charleston, WV

Dr. Gupta reports no financial relationships relevant to this field of study.

Synopsis: A study of patients with acute sore throat finds that a delayed prescription strategy prevents complications as effectively as immediate antibiotics, and that the delayed prescription approach is more effective than immediate antibiotics at reducing revisits.

Source: Little P, et al. Antibiotic prescription strategies for acute sore throat: A prospective observational cohort study. *Lancet Infect Dis* 2014;14:213-219.

ACUTE PHARYNGITIS, OR SORE THROAT, IS ONE OF THE MOST COMMON conditions encountered in an office practice in the United States. While bacterial (mostly group A streptococcus) etiology accounts for approximately only 10% of the total cases of pharyngitis and the major complications are rare, a majority of patients continue to receive presumptive antibiotic therapy.¹ Recent estimates demonstrate that as many as 60% of adults seen for a complaint of sore throat received an antibiotic prescription, with a trend toward prescribing broader-spectrum antibiotics (azithromycin) rather than narrow-spectrum antibiotics (penicillin).² Improper antibiotic prescribing is among several factors contributing to a growing epidemic of antibiotic resistance in the United States. In the clinical practice setting, physicians continue their efforts to reduce inappropriate antibiotic prescribing, including the use of clinically validated decision protocols when applicable. However, sometimes the avoidance of antibiotic prescribing in patients becomes a challenge, especially when concerns for clinical complications from pharyngitis are considered. Additionally, even when treating documented bacterial pathogens such as group A streptococcus, antibiotics may contribute minimally to the pace at which symptoms of pharyn-

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gitis resolve. Data from trials of antibiotics in acute pharyngitis suggest only moderate benefits in symptoms and prevention of complications.³ One strategy that seems to have had some success is the delayed provision of antibiotic prescriptions, in which the patient is prescribed an antibiotic that should be taken only in case of worsening of the symptoms or no improvement a few days after the visit. However, when evaluated scientifically, such studies have been underpowered to address symptom progression and complications.⁴

In their research, Little et al utilized a prospective, observational cohort study design involving 12,677 adult primary care patients in England and Wales who presented with a sore throat. Follow-up of the cohort was based on a detailed and structured review of the routine medical records and analysis of the comparison of three antibiotic prescription strategies (no antibiotic prescription, immediate antibiotic prescription, and delayed antibiotic prescription) to control for the propensity to prescribe antibiotics. A total of 4805 patients received no antibiotics, 6088 received antibiotics immediately, and 1784 received delayed prescriptions.

The researchers found that complications (such as otitis media and sinusitis) occurred in 164 of 11,950 patients (1.4%). In comparison with no antibiotic treatment, the risk of complications was 42% lower with delayed antibiotic treatment and 38% lower with immediate antibiotic treatment. The estimated number needed to treat (NNT) was 174 with delayed treatment and 193 with immediate antibiotic treatment. They also found

that the rate of re-consultation for new or unresolved symptoms was 39% lower with delayed antibiotics (NNT = 18) and 17% lower with immediate antibiotics (NNT = 40). In summary, the delayed prescription of antibiotics was associated with both a lower risk of complications and persistent symptoms than immediate prescription of antibiotics.

COMMENTARY

Antibiotic resistance has been called one of the world's most urgent public health challenges. There is no doubt that the number of bacteria resistant to antibiotics has increased in the past decade and several bacterial infections are becoming resistant to the most commonly prescribed antibiotic treatments. Primary care physicians see the bulk of upper respiratory tract infections, including pharyngitis, most of which are self-limiting, and antibiotics have only a minor impact on the course of most of these infections. In addition to resistance concerns, unrestricted antibiotic use has a number of disadvantages, including adverse effects, increased health care costs, and perhaps reinforcing a belief of usefulness in our patients that may not be entirely accurate.

Previous studies have demonstrated that delayed antibiotic prescription reduces antibiotic use without an increase in complications, with little advantage compared with the non-prescription strategy.³ However, the current research by Little et al demonstrates that although in most cases an antibiotic is not needed; delayed antibiotic prescription and no antibiotic prescription do not have comparable outcomes. If an antibiotic prescription is being considered, a delayed antibiotic prescription strategy is likely to provide at least a reduction in complications similar to an immediate antibiotic prescription, and perhaps with a reduced rate of revisits. The study also demonstrates that suppurative complications are relatively uncommon in primary care, although it remains difficult to predict who will develop those.

In summary, for patients presenting with typical acute sore throat, it is prudent to utilize a widely accepted clinical decision tool such as the Centor criteria to conduct

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Managing Editor, at (404) 262-5404.

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initial clinical evaluation and further testing.⁵ However, when a decision to prescribe an antibiotic is anticipated, the current study suggests that a strategy to utilize the delayed antibiotic treatment approach may also further the goal of addressing antibiotic resistance concerns. ■

References

1. Wessels MR. Clinical practice: Streptococcal pharyngitis. *N Engl J Med* 2011;364:648-655.
2. Barnett ML, Linder JA. Antibiotic prescribing to adults with sore throat in the United States, 1997-2010. *JAMA Intern Med* 2014;174:138-140.
3. Spinks A, et al. Antibiotics for sore throat. *Cochrane Database Syst Rev* 2013;(11):CD000023.
4. Arroll B, et al. Do delayed prescriptions reduce antibiotic use in respiratory tract infections? A systematic review. *Br J Gen Pract* 2003;53:871-877.
5. Centor RM, et al. The diagnosis of strep throat in the emergency room. *Med Decis Making* 1981;1:239-246.

Prognosis of First-Degree AV Block

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

Professor of Medicine, Lucie Stern Chair in Cardiology, Director, Cardiology Fellowship Program, Chief of Clinical Cardiology, University of California, San Francisco

Dr. Crawford reports no financial relationships relevant to this field of study. This article originally appeared in the March 2014 issue of Clinical Cardiology Alert.

Synopsis: *The authors concluded that in an apparently healthy, middle-aged population, a prolonged PR interval can normalize over time in almost one-third of subjects, and even if persistent, is not associated with death or cardiovascular morbidity and mortality.*

Source: Aro AL, et al. Prognostic significance of prolonged PR interval in the general population. *Eur Heart J* 2014;35:123-129.

ALTHOUGH LONG BELIEVED TO BE BENIGN, FIRST-DEGREE AV block has recently been shown to be associated with atrial fibrillation development, pacemaker need, and all-cause mortality. This group of investigators from Finland had access to a 30-year follow-up study of almost 11,000 apparently healthy, middle-aged Finns where the prognostic value of the ECG PR interval could be assessed. In 10,957 men and women aged 30-59 years at entry between 1966-1972, a complete history, targeted physical

examination, routine laboratory studies, and an ECG were done. They were followed for a mean of 30 ± 11 years until 2007. Less than 2% were lost to follow up. The endpoints of death, cardiovascular death, sudden death, and hospitalizations were obtained from Finland government data and medical record reviews. Also, a second ECG was performed after a mean of 6 years into the study.

A PR interval > 200 msec was observed in 2.1% of the subjects and was more common in obese older men and related to a slower heart rate and suspected cardiac disease. At the 6-year ECG, 71% of the subjects with a prolonged PR at entry still had it. After adjustment for age and sex, prolonged PR interval was not associated with all-cause cardiovascular or sudden death, and these results were not changed by multivariate adjustment, including use of a PR interval of > 220 msec. Also, the risk of hospitalization for atrial fibrillation, CAD, heart failure, or stroke did not differ from the rest of the population. The authors concluded that in an apparently healthy, middle-aged population, a prolonged PR interval can normalize over time in almost one-third of subjects, and even if persistent, is not associated with death or cardiovascular morbidity and mortality.

■ COMMENTARY

Occasionally, we see isolated PR interval prolongation on ECG in an otherwise healthy individual without overt cardiac disease and wonder if we should be concerned. This study in almost 11,000 middle-aged (30-59 years) subjects followed for a mean of 30 years sheds considerable light on the issue. When combined with prior studies, several conclusions can be reached. Overall, in an otherwise healthy, middle-aged population, first-degree AV block is not a harbinger of death, sudden death, or cardiovascular (CV) morbidity when adjusted for age, sex, and risk factors for CV disease. So why is the PR interval prolonged in some healthy people? It is related to heart rate and really should be adjusted for heart rate the way the QT interval is, but since this is only relevant at heart rates < 60 beats per minute we don't bother. It is influenced by autonomic nervous system tone. Increased PR can be seen in athletes and others with high vagal tone. It has a circadian variation, so the time of day the ECG is done can be important. These observations probably explain the disappearance of first-degree block in this study at the 6-year follow-up in about one-third of the population studied. There is also a genetic component and it can be associated with atrial arrhythmias and the development of AV block. This is not surprising because we know there is a large genetic influence on the risk of developing atrial fibrillation.

Clearly a prolonged PR interval can be a harbinger of future conduction system disease in some people, espe-

cially older subjects where cardiac degenerative diseases are more common. Also, if a patient develops diastolic dysfunction, a prolonged PR interval can adversely affect diastolic filling and lead to diastolic mitral valve regurgitation, which under the right conditions could contribute to the development of heart failure. So how should we handle patients with first-degree heart block? If they are young and overtly healthy, I would repeat the ECG in 1-3 years because it may just disappear with age or deconditioning. In older patients, it would prompt me to repeat the ECG at the time of their routine health maintenance follow-up exams, which is usually every 1-2 years depending on age. However, patients should be reassured that most people with this finding have normal longevity and are free from CV disease. ■

Immunization of Adults — Updates

ABSTRACT & COMMENTARY

By Stan Deresinski, MD, FACP, FIDSA

Clinical Professor of Medicine, Stanford University, Associate Chief of Infectious Diseases, Santa Clara Valley Medical Center

Dr. Deresinski does research for the National Institutes of Health, and is an advisory board member and consultant for Merck. This article originally appeared in the March 2014 issue of Infectious Disease Alert.

Synopsis: The recommendations for immunization of adults have been updated.

Source: Bridges CB, et al. Advisory committee on immunization practices recommended immunization schedule for adults aged 19 years or older – United States, 2014. *MMWR Morb Mortal Wkly Rep* 2014;63:110-112.

UPDATED STANDARDS FOR IMMUNIZATION OF ADULTS WERE approved by the National Vaccine Advisory Committee (NVAC) in September 2013.¹⁻³ Some of the changes made are as follows.

- Haemophilus influenzae type B (Hib) vaccine is now recommended for selected adults at increased risk of Hib infection who have not previously received the vaccine. Regardless of previous receipt, adult hematopoietic stem cell transplant recipients should receive three doses of Hib vaccine 6-12 months after vaccination. In contrast to previous guidance, it is no longer recommended that HIV-infected individuals be vaccinated against Hib as a result of recognition of their low risk of infection with this organism.

- Recombinant influenza vaccine contains no egg pro-

tein and can be administered to individuals 18 through 49 years of age with egg allergy of any severity. Either recombinant or inactivated influenza vaccine (which does contain egg protein) can be given to individual whose only allergic manifestation after egg protein exposure is urticaria.

- A single dose of Tdap vaccine is recommended for previously unvaccinated persons aged 11 years or older, and a Td booster should be administered every 10 years thereafter. Pregnant women continue to be recommended to receive 1 dose of Tdap vaccine during each pregnancy, preferably during 27-36 weeks' gestation, regardless of the interval since prior dose of Tdap or Td vaccine.

- Because the 13-valent conjugated pneumococcal vaccine (PCV13) is recommended to be administered before PPSV23 among persons for whom both vaccines are recommended, the PCV13 footnote now precedes the PPSV23 footnote and includes wording to remind providers of the appropriate order of these vaccines when both are indicated.

- The meningococcal vaccine footnote was edited to clarify which persons need either one or two doses of vaccine and to provide greater clarity regarding which patients should receive the meningococcal conjugate vs the meningococcal polysaccharide quadrivalent vaccines.

- No changes or minor clarifications were made to the MMR, hepatitis A, or hepatitis B vaccine footnotes; no changes in recommendations were made.

Vaccination levels of adults in the United States are disappointingly low. The NVAC recommends that providers assess vaccination needs for their patients at each visit, recommend needed vaccines, and then, ideally, offer the vaccine or, if the provider does not stock the needed vaccines, refer the patient to a provider who does vaccinate. Vaccination providers should also ensure that patients and their referring health care providers have documentation of the vaccination. ■

References

1. <http://www.cdc.gov/vaccines/schedules>.
2. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older: United States, 2014. *Ann Intern Med* 2014;160:190-197.
3. ACIP Adult Immunization Work Group, Bridges CB, et al. Centers for Disease Control and Prevention (CDC). Advisory Committee on Immunization Practices (ACIP) recommended immunization schedule for adults aged 19 years and older – United States, 2013. *MMWR Morb Mortal Wkly Rep* 2013;62(Suppl 1):9-19.

Ibrutinib Capsules (Imbruvica™)

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 relationships relevant to this field of study.

AN INHIBITOR OF BRUTON'S TYROSINE KINASE (BTK) HAS been recently approved for the treatment of chronic lymphocytic leukemia (CLL) for patients who have previously been treated. Ibrutinib, approved in November for mantle cell lymphoma (MCL), was approved under the FDA's accelerated approval process for treatment of CLL. It is marketed by Pharmacyclics, Inc., and Janssen Biotech as Imbruvica.

Indications

Ibrutinib is indicated for the treatment of MCL and chronic lymphocytic leukemia in patients who have received at least one prior therapy.¹

Dosage

The recommended dose is 560 mg orally once daily for MCL and 420 mg once daily for CLL. It is available as 140 mg capsules. The dose should be reduced if co-administered with a moderate 3A4 inhibitor that is clinically necessary.¹ The dose should be modified for adverse events.

Potential Advantages

Ibrutinib as monotherapy was able to achieve an overall response rate of 66% in MCL and 58% in CLL in previously treated patients.

Potential Disadvantages

Approximately one-half of patients experience some grade of bleeding with 5-6% grade 3 or higher. About 40% have grade 3 or higher cytopenia and about 30% have grade 3 infections. Common adverse events (> 25%) include diarrhea, nausea, constipation, fatigue musculoskeletal pain, and dyspnea. Other malignancies have been reported in 5% of MCL patients and 10% of CLL patients treated with ibrutinib, mostly skin cancers. Ibrutinib should not be given with a strong or moderate CYP3A4 inhibitor or strong CYP3A4 inducer.¹

Comments

Ibrutinib is an irreversible inhibitor of BTK that acts as a signaling molecule of the B-cell antigen receptor and cytokine receptor pathways.^{1,2} Its safety and efficacy was evaluated in 111 subjects with MCL and 48 subjects with CLL in open-label trials. Subjects with MCL were previously treated (median of three treatments), aged 68 years (40–84), median time since diagnosis was 42 months, 39% had at least one tumor 5 cm or larger, 49% had bone marrow involvement, and 54% had extranodal involvement. Ibrutinib was administered at 560 mg once daily until disease progression or unacceptable toxicity. The primary endpoint was investigator assessed overall response rate (ORR). ORR was 65.8% (95% confidence interval [CI], 56.2, 74.5). The complete response was 17.1% and partial response was 48.6%. The median time to response was 1.9 months with a duration of response of 17.5 months. For CLL, 48 subjects had a median time from diagnosis of 80 months and a median number of prior treatments of four, and 46% had at least one tumor of 5 cm or larger at baseline. Ibrutinib was administered as a once-daily dose of 420 mg. ORR (all partial) was 58.3% (95% CI, 43.2, 72.4). Transient increase in lymphocyte count (> 50%) occurred in 77% of CLL subjects and 33% of MCL subjects. The onset occurred in the first few weeks to first month of treatment and resolved by a median of 23 weeks in CLL subjects and 8 weeks in MCL subjects.

Clinical Implications

MCL is a rare form of non-Hodgkin lymphoma (NHL) representing 5-9% of new NHL.² It is a male predominant disease with allogeneic stem cell transplantation as the most effective therapy. For those in which this is not an option, other FDA-approved drugs include bortezomib (Velcade) and lenalidomide (Revlimid). Bortezomib showed an ORR of 31% and duration of response (DOR) of 9.3 months, while lenalidomide had an ORR of 26% and DOR of 16.6 months.³ Ibrutinib provides an active therapy for relapsed and refractory disease. CLL is also a rare blood and bone marrow disease characterized by an increase in B-lymphocytes. Current therapy includes fludarabine, cyclophosphamide, and rituximab. For untreated patients, the ORR was 95%.⁴ This combination is not recommended for relapsed/refractory disease. Preferred treatment includes combination chemotherapy.⁵ Ibrutinib offers a single-agent option in those patients. The wholesale cost of treatment of MCL is \$10,933 for 30 days and \$8,200 for CLL for 30 days. ■

References

1. Imbruvica Prescribing Information. Sunnyvale, CA: Pharmacyclics, Inc.; February 2014.

2. Wang ML, et al. Targeting BTK with ibrutinib in relapsed or refractory mantle-cell lymphoma. *N Engl J Med* 2013;369:507-517.
3. http://www.accessdata.fda.gov/drugsatfda_docs/nda/2013/205552Orig1s000SumR.pdf. Accessed March 25, 2014.
4. Keating MJ, et al. Early results of a chemoimmunotherapy regimen of fludarabine, cyclophosphamide, and rituximab as initial therapy for chronic lymphocytic leukemia. *J Clin Oncol* 2005;23:4079-4088.
5. <https://www5.medicine.wisc.edu/~williams/nhl.pdf>. Accessed March 25, 2014.

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CME Questions

1. In the study by Little et al, researchers found that in comparison with no antibiotic treatment for acute pharyngitis, the risk of complications was:
 - a. 58% lower with immediate antibiotic treatment.
 - b. 42% lower with delayed antibiotic treatment.
 - c. 42% lower with immediate antibiotic treatment.
 - d. 58% lower with delayed antibiotic treatment.
2. In a general, apparently healthy population, a prolonged PR interval:
 - a. is common.
 - b. is associated with sudden cardiac death.
 - c. is associated with atrial fibrillation development.
 - d. resolves over time in one-third.
3. The National Vaccine Advisory Committee recommends that:
 - a. providers assess vaccination needs for their patients at each visit.
 - b. providers recommend needed vaccines.
 - c. providers offer the vaccine, or if the provider does not stock the needed vaccines, refer the patient to a provider who does vaccinate.
 - d. All of the above

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is a retained consultant for Boehringer Ingelheim, Daiichi Sankyo, Forest Pharmaceuticals, Janssen, Lilly, Novo Nordisk, Pfizer, and Sanofi.

CV Hope for the Exercise-Disinclined

Source: Kearney TM, et al. Accumulated brisk walking reduces arterial stiffness in overweight adults: Evidence from a randomized control trial. *J Am Soc Hypertens* 2014;8:117-126.

THE FAVORABLE RELATIONSHIP BETWEEN exercise and cardiovascular health has been announced, and reannounced, and reannounced for decades. Nonetheless, only a minority of Americans participate in regular vigorous exercise, and the numbers of adult Americans who are categorized as overweight or obese continues to climb. Does one have to be an athlete to claim the rewards of physical activity? Maybe not.

Kearney et al performed a study among overweight adult men and women who acknowledged being essentially sedentary. Subjects randomized to exercise were compared to subjects performing stretching activities, with the outcome of interest being the effects on vascular health as measured by arterial stiffness (reflected in pulse wave velocity) and production of nitric oxide.

It is the novelty of the applied exercise program that might strike clinicians as having potential for widespread use: The exercise subjects were asked to engage in three 10-minute sessions of brisk walking on 5 days of each week. Brisk walking was described as sufficient to produce slight shortness of breath but not impede the ability to hold a conversation. Outcomes were measured at the end of the 6-month intervention, and 4 months after the intervention ended.

At study end, as well as 4 months post-intervention, there was a statistically significant difference in pulse-wave velocity and nitric oxide production in the exercise group compared to the stretching group. Even for those with too-busy schedules, lack of athletic prowess, and distaste for overly strenu-

ous activity, a menu of brief episodes of brisk walking for only 5 days per week might be an attractive option. ■

The Elbow Sign for OSA

Source: Fenton ME, et al. The utility of the elbow sign in the diagnosis of OSA. *Chest* 2014;145:518-524.

OBSTRUCTIVE SLEEP APNEA (OSA) IS GAINING ever-growing respect from clinicians who recognize it is responsible for diverse toxicities beyond simple sleep disruption: hypertension, cardiac arrhythmia, auto accidents, and excessive daytime sleepiness among them. Clinicians tend to uncover OSA when persons of “typical” phenotype (overweight mid-life men and women) present with associated symptoms. Sometimes, the consequence of OSA triggers an evaluation, even in the absence of overt OSA symptoms, such as the recent observation that among persons with resistant hypertension and no history or overt stigmata of OSA, sleep studies were positive for OSA in more than 80%!

Not everyone can afford a sleep study, so clinicians would like to identify simple methods to refine the pretest probability of OSA. The elbow sign may be just such an intervention.

Fenton et al provide data on asking patients referred for a sleep study two questions: 1) Does your bed partner ever poke or elbow you because you are snoring? or 2) Does your bed partner ever poke or elbow you because you have stopped breathing?

Persons who answered affirmatively to either question were 4-6 times more likely to emerge with sleep studies that were positive for OSA. Correction for other OSA-related items (body mass index, Epworth Sleepiness Scale, etc.) did not alter this relationship.

These two simple questions may help identify patients most likely to benefit from a sleep study investigation. ■

Another New and Underrecognized Psoriasis Comorbidity

Source: van der Voort EA, et al. Psoriasis is independently associated with non-alcoholic fatty liver disease in patients 55 years old or older: Results from a population-based study. *J Am Acad Dermatol* 2014;70:517-524.

UPON ENCOUNTERING THE WORD psoriasis, clinicians typically first think “skin,” and might next reflect on “joints,” and perhaps even “nails,” but rarely does the internal intellectual discussion go any further. It is only in the last decade that an immunologically related disorder — rheumatoid arthritis — has been recognized to be associated with marked increase for cardiovascular (CV) disease. More recently, an association between psoriasis and CV disease has also been confirmed, and although the mechanism by which either of these inflammatory disorders induces vasculopathy is unclear, their common immunologic underpinnings suggest shared pathology.

According to a report by van der Voort et al, we should consider adding nonalcoholic fatty liver disease (NAFLD) to the list of comorbidities related to psoriasis. Reflecting on earlier case-control studies that indicated an increased prevalence of NAFLD among psoriasis patients, the authors studied a large population of persons enrolled in the Rotterdam Study (n = 2292) who underwent hepatic ultrasound. The prevalence of NAFLD was more than 30% greater in psoriasis subjects than controls (46.2% vs 33%).

The mechanism by which NAFLD is induced by psoriasis is unclear, although specific culprit genes are suspected. Because most of these patients did not have severe psoriasis, clinicians should be vigilant for the potential development of NAFLD, even in psoriatic patients with mild-moderate disease. ■

Is the Right Atrium Enlarged?

By Ken Grauer, MD, Professor Emeritus in Family Medicine, College of Medicine,
University of Florida

Dr. Grauer is the sole proprietor of KG-EKG Press, and publisher of an ECG pocket brain book.

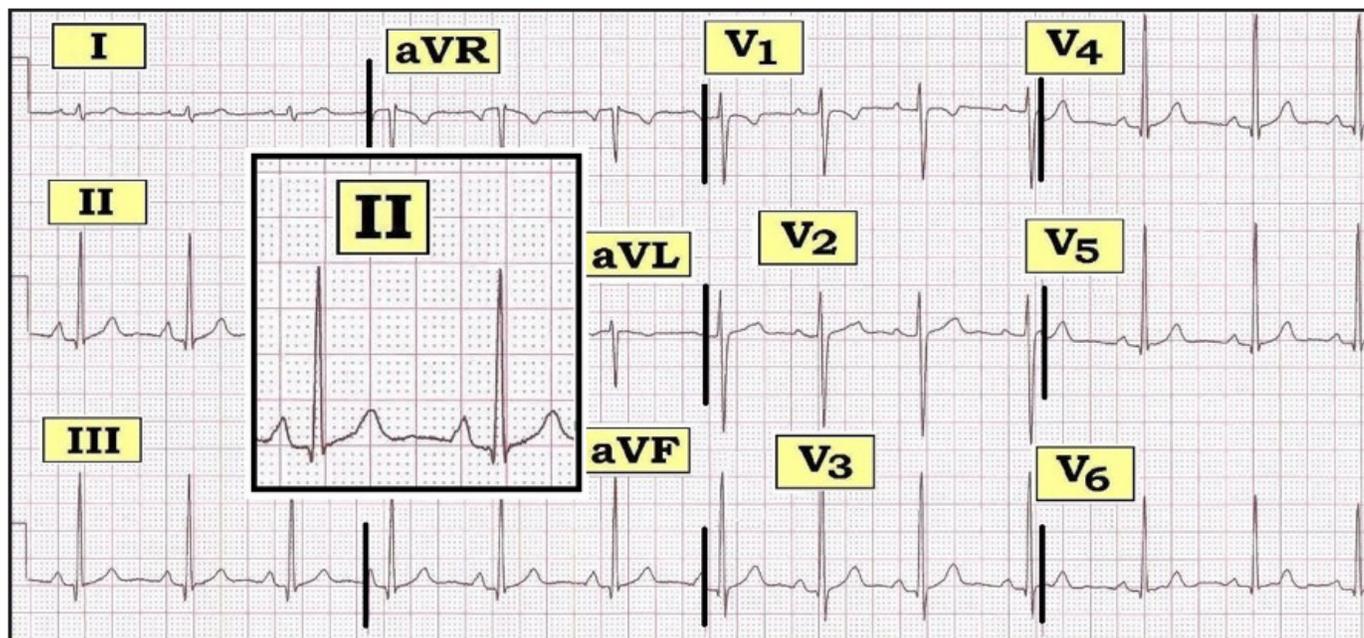


Figure — ECG from a 27-year-old man. Is there right atrial enlargement?

Scenario: The 12-lead ECG in the Figure was obtained from a 27-year-old man. Does the patient have a large right atrium?

Interpretation: The ECG shows sinus arrhythmia with a “vertical” axis that we estimate to be about +80 degrees (the QRS is much more positive in lead aVF than it is in lead I). There are small, narrow q waves in multiple leads. QRS amplitude is probably not increased given the young age of this adult. The insert highlights the P wave in lead II, which is at least 3 mm tall and pointed. This satisfies criteria for right atrial abnormality (RAA). Otherwise, all findings on this tracing might be normal if this 27-year-old man was asymptomatic with a normal physical exam.

Many clinicians interchange the terms LAA/RAA and LAE/RAE. We prefer the terms “LAA” and “RAA” — where the second letter “A” stands for left and right atrial “abnormality.” Given the poor sensitivity and specificity of ECG for assessing atrial dimensions — use of the designations LAA/RAA allows us to acknowledge unusual P wave morphology on ECG that may not necessarily correlate with true anatomic atrial “enlargement.” Reasons for

abnormal P wave morphology not due to atrial chamber enlargement include atrial conduction defects, increased atrial pressure (as may occur in patients with acute heart failure), and body habitus. For example, it is not uncommon to see peaked inferior P waves in otherwise healthy young adults who have a relatively vertical mean QRS axis. We suspect this is what we are seeing in the Figure.

Clearly, clinical history and awareness of physical exam findings would be needed to know for certain what (if anything) the tall and pointed inferior P waves in the Figure mean. It turned out that this patient was slender, asymptomatic, and had a normal exam (no heart murmur). This ECG was performed for routine indication related to a job rather than because of symptoms. Under these circumstances, designation of “RAA” allows us to acknowledge unusual P wave appearance *without* necessarily attributing this to any cardiac pathology in this 27-year-old man who probably has a normal heart.

For more information on right atrial abnormality, please visit: <http://ecg-interpretation.blogspot.com/2013/09/ecg-interpretation-review-75-chamber.html>. ■

INTERNAL MEDICINE ALERT

2014 Internal Medicine Alert Reader Survey

In an effort ensure *Internal Medicine Alert* is addressing the issues most important to you, we ask that you take a few minutes to complete and return this survey. The results will be used to ensure you are getting the information.

Instructions: Mark your answers by filling in the appropriate bubbles. Please write your answers to the open-ended questions in the space provided. Either fax the completed questionnaire to 404-492-5933, or return it in the enclosed postage-paid envelope. The deadline is July 1, 2014.

In future issues of *Internal Medicine Alert*, would you like to see more or less coverage of the following topics?

- | | A. more coverage | B. less coverage | C. about the same |
|-------------------------|-------------------------|-------------------------|-------------------------|
| 1. Endocrinology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 2. Pulmonology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 3. Cardiology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 4. Dermatology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 5. Neurology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 6. Gastroenterology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 7. Rheumatology | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 8. Men's Health | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 9. Women's Health | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 10. Pediatrics | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |
| 11. Preventive Medicine | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C |

12. What other topics would you like to see discussed in *Internal Medicine Alert*? _____

13. Are the articles in *IMA* written about issues of importance and concern to you?

- A. always B. most of the time C. some of the time D. rarely E. never

14. Are the articles in *Internal Medicine Alert*

- A. Too short B. Too long C. About right

15. What type of information not currently provided in *Internal Medicine Alert* would you like to see added? _____

Please rate your level of satisfaction with the the items listed: Please mark your answers in the following manner:

- | | A. excellent | B. good | C. fair | D. poor |
|----------------------------|-------------------------|-------------------------|-------------------------|-------------------------|
| 16. quality of newsletter | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |
| 17. article selections | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |
| 18. timeliness | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |
| 19. quality of commentary | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |
| 20. clearness of abstracts | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |
| 21. overall value | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |
| 22. customer service | <input type="radio"/> A | <input type="radio"/> B | <input type="radio"/> C | <input type="radio"/> D |

23. To what other publications or information sources about internal medicine do you subscribe?

24. Including *IMA*, which publication or information source do you find most useful, and why?

25. Please describe your work place:

- A. private practice B. hospital C. government institution D. research
 E. Other _____

26. In the future, how do you plan to obtain your CME and CNE credits?

- A. travel to live conferences B. subscription-based newsletters/journals C. outside-sponsored teleconferences
 D. Internet-based activities E. Other (please specify) _____

27. List the top three challenges you face in your job today:

Contact information _____
