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Missed ED Diagnosis of Acute Coronary Syndrome

ABSTRACT & COMMENTARY

Source: Pope JH, et al. Missed diagnosis of acute cardiac ischemia in the emergency department. *N Engl J Med* 2000;342:1163-1170.

The acute cardiac ischemia time-insensitive predictive Instrument (ACI-TIPI) trial, which served as the database for this paper, included data from 10 major centers on more than 10,000 patients age greater than 30 who presented to the ED with angina or anginal-equivalent symptoms. The authors sought to determine the incidence of failure to admit patients with acute coronary syndromes (ACS), defined as either acute myocardial infarction (AMI) or unstable angina. Analyzing these cases, they set out to identify factors related to the failure to admit and to review the clinical outcomes of those patients who were mistakenly discharged.

In this trial, patients who were not admitted returned within 24-72 hours. Data were available on 99% of these patients, providing a good information source. One thousand eight hundred sixty-six of 10,689 patients (17%) met the criteria for ACS; 894 had AMI (8%) and 972 had unstable angina (9%). Excluding those patients leaving against medical advice (11 in total), 19 of 889 (2.1%) had a missed AMI, and 22 of 966 (2.3%) had unstable angina. The chart for one of those patients was not available.

Review of the medical records of these 40 patients revealed the following key points:

- ED attendings saw more than 82.5% (but not all) of these patients.
- Two of 19 AMI patients had ECGs that were misread by the ED physician.
- Fourteen (74%) of 19 patients with AMI had non-Q wave infarctions.
- 53% of AMI patients and 62% of unstable angina patients had normal or non-diagnostic ECGs.

Multivariate analyses for all ACS patients revealed the following independent predictors of inappropriate discharge:

- female gender with age less than 55;
- nonwhite race;

INSIDE

• chief complaint of dyspnea (rather than chest pain);
• normal ECG.

A slight, statistically nonsignificant trend toward a higher risk-adjusted death rate was found in those patients with ACS who were discharged.

COMMENT BY RICHARD A. HARRIGAN, MD, FAAEM

How you interpret these findings may depend upon whether you typically see the glass as half-full or half-empty. The accompanying editorial emphasizes that the miss rate in this study is consistent with the findings in a number of earlier studies.[1] Of course, if you are one of the 2.1% of patients discharged with an AMI (or one of the physicians discharging), the company you keep is of little consolation. One number that should have certainly improved since these data were gathered in 1993 is the number of patients not seen by an attending ED physician. This number should now be zero at all institutions that do not rely on resident moonlighting. The authors point out that well-established chest pain centers did not fare better in this trial. However, the current state of serum cardiac markers and cardiac imaging has advanced since that time, and one hopes this would have a positive influence on inappropriate discharge rates.[2] ❖

References

1. Mehta RH, Eagle KA. Missed diagnosis of acute coronary syndromes in the emergency room—Continuing challenges. *N Engl J Med* 2000;342:1207-1209.
2. Lee TH, Goldman L. Evaluation of the patient with acute chest pain. *N Engl J Med* 2000;342:1187-1195.

A Shorter Antibiotic Course for Pyelonephritis?

ABSTRACT & COMMENTARY

Source: Talan DA, et al. Comparison of ciprofloxacin (7 days) and trimethoprim-sulfamethoxazole (14 days) for acute uncomplicated pyelonephritis in women. *JAMA* 2000;283: 1583-1590.

In a multicenter, randomized, double-blind, outpatient trial in women ages 18 or older, the efficacy of a seven-day course of ciprofloxacin (500 mg bid) was compared to a 14-day course of trimethoprim-sulfamethoxazole (TMP-SMX) (160 mg/800 mg bid) for uncomplicated acute pyelonephritis. The diagnosis was established by the usual clinical findings and substantiated by fixed microscopic pyuric criteria. Of the three hundred seventy-eight patients enrolled, 120 were ultimately excluded from efficacy data analysis because of reasons that included the following: no causative organism on culture; inadequate study drug consumption; lost to follow-up; or other miscellaneous protocol violations. Ultimately, the ciprofloxacin group (n = 128) and TMP-SMX group (n = 127) were found to have similar demographic and clinical characteristics. Treating physicians were allowed discretion regarding whether to administer a first dose of intravenous antibiotics (ciprofloxacin in the 7-day ciprofloxacin group vs ceftriaxone in the 14-day TMP-SMX group). Primary outcome measures included drug efficacy as assessed by bacteriologic and clinical cure both during and after completion of therapy. Secondary measures included adverse drug reactions, organism resistance patterns, continued bacteriologic and clinical cures, and cost analyses.

Not surprisingly, *Escherichia coli* was the most common causative organism, being isolated in more than 90% of cultures in both study groups. Eighteen percent of all uropathogens isolated were resistant to TMP-SMX, however, including 44 instances of *E. coli* resistance. Only one isolate was resistant to ciprofloxacin (1 of 3 cultured *Proteus mirabilis* pathogens). Among the *E. coli*

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resistant to TMP-SMX, there was marked regional variation: Eastern sites, 7%; Midwestern, 14%; and Western, 32%. With respect to bacteriologic cure, 99% of the ciprofloxacin group achieved cure during the 4- to 11-day post-therapy visit, as opposed to 89% of the TMP-SMX group (95% CI, 0.04-0.16; P = 0.004). Regarding clinical outcome, 96% of the ciprofloxacin group had continued clinical cure through the 4- to 11-day post-therapy visit, in contrast to 83% of the TMP-SMX group (95% CI, 0.06-0.22; P = 0.002). In those patients with data available at a second, later point in time (22- to 48-day post-therapy visit), the shorter-course ciprofloxacin again prevailed, although the bacteriologic cure difference did not reach statistical significance. Bacteriologic cure was achieved in 85% of the ciprofloxacin-treated patients vs. 74% of the TMP-SMX-treated patients (95% CI, 0.00-0.21; P = 0.08), whereas clinical cure was found in 91% of the ciprofloxacin group as opposed to 77% of the TMP-SMX group (95% CI, 0.03-0.23; P = 0.02). The bacteriologic and clinical cure rates of those who did receive an initial intravenous dose of antibiotic were compared to the cure rates of those who did not. Clinical cure rates were similar in both groups regardless of whether a dose of intravenous antibiotic was given. Bacteriologic cure rates were similar for the ciprofloxacin group regardless of intravenous augmentation, but the TMP-SMX group had a higher bacteriologic cure rate at the 4- to 11-day visit, an advantage that was not maintained through the 22- to 48-day encounter.

Adverse events tended to be more common in the TMP-SMX group (33%) than the ciprofloxacin group (24%); this difference persisted when comparing events that led to discontinuation of the study drug (6% in the ciprofloxacin group vs 11% in the TMP-SMX group). Despite the higher cost of ciprofloxacin, aggregate costs were higher in the TMP-SMX-treated patients because of a greater number of clinical failures.

The authors conclude that a seven-day course of ciprofloxacin is at least as efficacious as a 14-day course of TMP-SMX for outpatient treatment of uncomplicated pyelonephritis in women, with the quinolone actually demonstrating statistical superiority. They caution that these findings cannot be extrapolated to men or to patients who have complicated infections or severe sepsis.

COMMENT BY RICHARD A. HARRIGAN, MD, FAAEM

This is an important study conducted by some of the leading researchers in the fields of infectious disease in emergency medicine (Talan and Moran) and urinary tract infection (Stamm and Hooton). As the authors point out, the issue of whether we can treat outpatient pyelonephritis for fewer than 14 days has not been well studied. In that it is a disease not only of the urine but also of medullary renal tissue, adequate serum levels of drug (which correlate with in vitro sensitivity) may be necessary to terminate the infection. This is in contradistinction to simple cystitis, where high levels of drug in the urine may supersede in vitro resistance issues. This study demonstrated that in vitro resistance to TMP-SMX was strongly associated with bacteriologic and clinical treatment failures.

The geographic patterns of resistance found in this study should be noted. Similarly, a high rate of *E. coli* resistance was noted in another recent study of cystitis conducted in the Northwest that was reviewed previously in *Emergency Medicine Alert*.[1] *(See* Emergency Medicine Alert, *May 1999, p. 90.)* Fluoroquinolones should be considered the treatment of choice in regions demonstrating significant resistance (i.e., > 10% of isolates) to TMP-SMX.[2] Treatment with TMP-SMX, if employed, should be conducted with particular attention to urine culture and sensitivity results. Complicated pyelonephritis (e.g., in diabetics, males, structural/functional urologic abnormalities, nursing home patients) is a different entity; the treating physician must be wary of polymicrobial infection and related issues of antibiotic resistance.[2] ❖

References

1. Gupta K, et al. Increasing prevalence of antimicrobial resistance among uropathogens causing acute uncomplicated cystitis in women. *JAMA* 1999;281:736-738.
2. Talan DA. New concepts in antimicrobial therapy for emergency department infections. *Ann Emerg Med* 1999;34:503-516.

Ketamine and Midazolam for Procedures in Adults

ABSTRACT & COMMENTARY

Source: Chudnofsky CR, et al. A combination of midazolam and ketamine for procedural sedation and analgesia in adult emergency department patients. *Acad Emerg Med* 2000;7:228-235.

Ketamine is used widely for pediatric conscious sedation and analgesia during painful ED procedures. Its use in adults, however, has been limited because of concerns regarding adverse and emergence reactions. In this prospective, observational study, the authors report their experience using ketamine with midazolam for procedural sedation in adult ED patients.

The investigators studied vital signs, adequacy of sedation using an alertness scale, adverse effects, emergence reactions, patient satisfaction, and time to attainment of discharge alertness. Data were collected prospectively by respiratory therapists who monitored patients during procedure and recovery, although physicians verified any adverse reactions. Severity of emergence reactions was graded based on retrospective chart review.

The authors report on 70 patients (ages 18-68 years) who received intravenous ketamine (2 mg/kg) after midazolam (0.07 mg/kg) for sedation prior to painful procedures (primarily incision and drainage or fracture/joint reduction). Adequacy of sedation was excellent, with mean ketamine doses of 159 mg and midazolam doses of 5.6 mg. Seven patients (10%) suffered adverse effects, including respiratory depression (4 patients), vomiting (2 patients), and myoclonia (1 patient). These effects were transient and easily treated (by oral airway or brief assisted bagging for respiratory depression) and did not affect disposition. Five patients (7%) experienced mild emergence reactions, including anxiety (2 patients), euphoria (2 patients), and calling out during recovery (1 patient). Eighteen patients (26%) recalled dreaming, but only five (7%) described the dreams as unpleasant. There was an increase in systolic blood pressure (mean increase of 26 mmHg), diastolic blood pressure (19 mmHg), and heart rate (21 bpm). All patients but one were satisfied and would choose the same sedation regimen. Mean time to discharge alertness was 64 minutes (range, 20 to 130 minutes). Based on their findings, the authors conclude this combination provides effective and safe procedural sedation and analgesia for adult ED patients.

COMMENT BY THEODORE C. CHAN, MD, FACEP

Ketamine causes dissociation between the cortical and limbic systems, resulting in profound sedation and analgesia while maintaining respiratory reflexes. While its use in children has been successful, experience with adults in this country has been limited. This study provides one of the largest case reviews of the adult use of ketamine with midazolam and strongly suggests the combination is safe and effective for procedural sedation.

However, a few points of caution must be considered. First, by inhibiting catecholamine reuptake, ketamine acts as a sympathomimetic agent and should be used with caution in those with ischemic heart disease, hypertension, or other cardiac risk factors, as well as in those of older age. Second, while midazolam reduces the incidence of emergence reactions, the combination should be avoided in those with a history of psychosis (including drug-induced psychosis), who may be at higher risk for developing these types of adverse reactions. Finally, while respiratory compromise is rare with ketamine, excessive doses of midazolam may result in significant respiratory depression, as seen in 6% of patients in this series (all of whom weighed > 97 kg and received correspondingly large doses of midazolam). The authors' cautionary note that such large doses of this medication in combination with ketamine should be avoided seems prudent. ❖

Special Feature

The New Fluoroquinolones

By Richard A. Harrigan, MD, FAAEM

Pharmacology is a rapidly changing field, with new drugs entering the market seemingly each week. Maintaining an up-to-date working knowledge of antibiotics is especially challenging to the emergency physician. Not only is the antibiotic armamentarium swiftly expanding, but bacterial sensitivity to existing antibiotics also is a dynamic construct. Perhaps one of the most rapidly developing groups of antimicrobials is the fluoroquinolone (FQ) class, with the last 12 months seeing the withdrawal from the market of two relatively new agents (grepafloxacin and trovafloxacin) and FDA approval of a pair of new FQs (moxifloxacin and gatifloxacin). The following review will focus on the newest FQ antibiotics: sparfloxacin; levofloxacin; moxifloxacin; and gatifloxacin. The salient differences with regard to absorption, elimination, drug interactions, adverse effects, and toxicity will be reviewed for these newer agents, highlighting similarities and differences with respect to earlier-generation FQs.

Fluoroquinolones: Background and General Characteristics

Descending from nalidixic acid, the FQs have evolved through several "generations." They share a common bicyclic structural base, with varying side chain substitutions leading to different (and improved) pharmacologic activity and new profiles regarding absorption, elimination, and adverse effects.[1] There is some variability in the literature regarding classification of these agents into generations;[1,2] awareness of the specific generation is less important than an understanding of the differences between the newer and older agents.

All FQs act by inhibiting the activity of DNA gyrase, which subsequently leads to impaired bacterial replication and rapid cell death.[1] They are bactericidal. Interestingly, they exhibit little cross resistance with other antibiotics,[1] which may be advantageous, yet can lead to

surprising cases of isolated FQ resistance, too.[3] *(See related story in this issue, p. 6.)* Intra-class cross-resistance should not be assumed, either.[1]

The newer FQs are notable for their enhanced antimicrobial activity, broader clinical indications, longer duration of effect (leading to less frequent administration), and high cost. *(See Table 1.)* The newer agents feature improved activity against gram-positive, anaerobic, and atypical pathogens.[2] Older FQs (e.g., ciprofloxacin, norfloxacin, and ofloxacin) have well-established roles in the treatment of urinary tract infections, sexually transmitted diseases, and in some cases (e.g., ciprofloxacin) inflammatory diarrhea. The newer agents all feature the FDA-approved indications of acute exacerbation of chronic bronchitis and community-acquired pneumonia. Indications shared by sparfloxacin and moxifloxacin are limited to these, whereas gatifloxacin and levofloxacin have broader indications that include these two syndromes. All new FQs are active against the most common pathogens seen in community-acquired pneumonia: *Streptococcus pneumoniae, Haemophilus influenzae, Chlamydia pneumoniae, Mycoplasma pneumoniae,* and *Moraxella catarrhalis*.[4] Indeed, levofloxacin is the first agent to be granted FDA approval for penicillin-resistant pneumococcus in patients with community-acquired pneumonia.[5]

Table 1

The New Fluoroquinolones: Cost*

Sparfloxacin (Zagam)	$76.65
Levofloxacin (Levaquin)	$85.34
Moxifloxacin (Avelox)	$87.12
Gatifloxacin (Tequin)	$72.87

* reflects average wholesale price for 10-day course of therapy

Absorption / Metabolism / Elimination

In general, FQs offer excellent oral absorption and high bioavailability that is only mildly affected by food.[6] Some older FQs (ciprofloxacin, enoxacin, norfloxacin) are bound by calcium, and thus should not be co-administered with milk or milk products. This is not a problem with the new FQs.[7-10] All FQs are chelated by other divalent cations, however, and the prescribing physician must be aware of interactions with magnesium, aluminum, iron, and zinc. The relevant medications in this regard include magnesium- or aluminum-containing antacids, multivitamins, iron supplements, buffered didanosine (Videx), and sucralfate (Carafate).[7-10] Table 2 contains information on the time delay intervals to be observed if these cationic preparations must be co-administered with FQs. *(See Table 2.)* For the two agents available as intravenous preparations (levofloxacin and gatifloxacin), infusions containing magnesium cannot share the same line.

Metabolism and elimination vary among the FQs. Levofloxacin is the best for use in hepatic insufficiency, in that 87% is excreted unchanged in the urine.[9] The other new FQs should not be used in moderate-to-severe (moxifloxacin) or severe (sparfloxacin, gatifloxacin) liver dysfunction.[7,8,10] All new FQs require a dosage adjustment based on creatinine clearance except moxifloxacin, which can be administered without dose modification. For sparfloxacin and levofloxacin, this adjustment begins when the creatinine clearance is less than 50 mL/min; for gatifloxacin, the threshold is less than 40 mL/min.[7,10,11]

Table 2

Cation Dosage Separation[7-10]

Sparfloxacin	4 h/4 h*
Levofloxacin	2 h/2 h*
Moxifloxacin	4 h/8 h*
Gatifloxacin	4 h/4 h*

* Administer oral dose at least x hours before / y hours after cation-containing agent

Drug Interactions

Another advantage of the new FQs is the relative lack of drug-drug interactions. Unlike ciprofloxacin, these agents do not increase theophylline levels. As discussed above, there is the chelation effect when co-administered with divalent cationic preparations (except calcium—again, however, a problem with ciprofloxacin). Sparfloxacin, moxifloxacin, and gatifloxacin all carry warnings regarding prolongation of the QT interval on the electrocardiogram. Thus, they should not be used with type Ia (e.g., quinidine, disopyramide, procainamide) or type III (e.g., sotalol, amiodarone) antiarrhythmics, and should be used with "significant caution" with erythromycin, cisapride, tricyclic antidepressants, or certain antipsychotics. It follows that these agents should not be used in instances of congenital long QT syndromes or metabolically mediated prolongation of the QT interval (e.g., hypokalemia, hypomagnesemia). The issue of QT prolongation and sporadic reports of torsade de pointes led Glaxo Wellcome to voluntarily withdraw grepafloxacin from the market in October 1999. Levofloxacin stands alone as the only new FQ that does not feature QT prolongation precautions.[7-11]

Toxicity

The new FQs are generally well-tolerated. Their most common side effects are gastrointestinal (e.g., nausea,

emesis, diarrhea), followed by neurologic (headache, dizziness, sleep disturbances, and rare seizures or mental status/psychotic changes).[1,12] All FQs carry the risk of phototoxicity, but this appears to be most significant with sparfloxacin, with a reported incidence of 8%. This can be severe, and patients are advised to avoid direct and filtered sunlight while on sparfloxacin and for five days after discontinuation of the drug.[1,10,12] Renal insufficiency and abnormal liver function tests have also been reported with the FQs.[1,12] Severe hepatotoxicity, including some deaths, led to the recent withdrawal of trovafloxacin from the market. As with the early-generation agents, the newer FQs are not recommended in pregnant or in pediatric/growing adolescent patients. Damage to juvenile articular cartilage in animal models is the basis for this recommendation; reports from children given FQs for compassionate reasons (e.g., infectious complications of cystic fibrosis) seem promising, however.[12]

FQ tendonopathy has been reported with a number of agents. Characteristically occurring within two weeks of initiation of FQ therapy (but a latency of up to 3 months has been described), the onset is often sudden. Painful swelling along the tendon sheath may be seen, and up to 50% of cases are bilateral. Although any tendon may be involved, there seems to be a predilection for high-stress tendons (e.g., calcaneal, quadriceps). Rupture can occur. Associated risk factors appear to include age, renal failure, corticosteroid use, and previous FQ tendonopathy. Treatment includes discontinuing the FQ (if still on it), splinting, and rest.[13]

Summary

The FQ class of antibiotics is rapidly evolving, with four late-generation agents (sparfloxacin, levofloxacin, moxifloxacin, and gatifloxacin) entering the market in recent times, plus two late-generation agents (trovafloxacin and grepafloxacin) having been withdrawn. The new FQs are quite different from early-generation FQs in many respects. Although these new agents share some commonality, they possess variable properties regarding absorption, elimination, drug interactions, and adverse effects. The emergency physician should be familiar with these individual agents, as they are likely to assume a significant role in the treatment of infectious disease. ❖

References

1. Blondeau JM. Expanded activity and utility of the new fluoroquinolones. *Clin Therapeutics* 1999;21:3-40.
2. Talan DA. New concepts in antimicrobial therapy for emergency department infections. *Ann Emerg Med* 1999;34:503-516.
3. Kemper CA. Levofloxacin-resistant pneumococci. *Infect Dis Alert* 2000;19:104.
4. Mandell LA. Antibiotic therapy for community-acquired pneumonia. *Clin Chest Med* 1999;20:589-598.
5. FDA approves new indication for Levaquin (levofloxacin tablet/injection). http://www.mdconsult.com.
6. Turnidge J. Pharmacokinetics and pharmacodynamics of fluoroquinolones. *Drugs* 1999;58 (Suppl 2):29-36.
7. *Avelox Product Information.* Bayer corporation. December 1999.
8. Perry CM, et al. Gatifloxacin. *Drugs* 1999;58:683-696.
9. Langtry HD, Lamb HM. Levofloxacin. *Drugs* 1998;56: 487-515.
10. *Zagam Product Information.* Rhone-Poulenc Rorer. October 1998.
11. *Tequin Product Information.* Bristol-Myers Squibb. January 2000.
12. Lipsky BA, Baker CA. Fluoroquinolone toxicity profiles: A review focusing on newer agents. *Clin Infect Dis* 1999;28:352-364.
13. Harrell RM. Fluoroquinolone-induced tendonopathy: What do we know? *South Med J* 1999;92:622-625.

Infectious Disease Update

Levofloxacin-Resistant Pneumococci

By Carol A. Kemper, MD, FACP
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Source: Wortmann GW, Bennett SP. *Clin Infect Dis* 1999; 29:1599-1600.

A 58-year-old man with a history of splenectomy was hospitalized in Washington, DC, with fever and sinusitis. He received levofloxacin, but became increasingly lethargic and died. Cultures of CSF yielded *Streptococcus pneumoniae* susceptible to penicillin, but no zone of inhibition to levofloxacin was seen on Etest. This unfortunate case serves as a harsh reminder that a small percentage of *S. pneumoniae* are resistant to levofloxacin.

While resistance to the macrolides, clindamycin, trimethoprim-sulfamethoxazole, and tetracycline is significantly increased in penicillin-resistant strains, it is important to recognize that the likelihood of quinolone resistance is independent of penicillin resistance.

Therefore, no inference can be made regarding the susceptibility of a penicillin-sensitive strain of *S. pneumoniae* to the quinolones. Recent susceptibility data for the United States of 2752 clinical isolates collected between 1996 and 1997 found that, on the basis of MIC data, grepafloxacin was the most active agent against *S. pneumoniae*, followed by sparfloxacin, levofloxacin, ciprofloxacin, and ofloxacin in descending order of activity (Thornsberry C, et al. *Antimicrob Agents Chemother* 1999;43:2612-2623). Nonetheless, ~0.2% of strains were resistant to levofloxacin or grepafloxacin with an MIC more than 2.0 mcg/mL. However, a recent report from Hong Kong identified a 5.5% resistance rate to levofloxacin among multiple drug-resistant strains of pneumococci (Ho PL, et al. *Antimicrob Agents Chemother* 1999;43:1310-1313). The newer quinolones should, therefore, not be used for cases of invasive or life-threatening streptococcal disease, irrespective of penicillin susceptibility data, unless their susceptibility to these agents has been predetermined. ❖

CME Questions

1. **Which of the following was found to be superior to a 14-day course of trimethoprim-sulfamethoxazole in the treatment of uncomplicated pyelonephritis in women?**
   a. A seven-day course of ciprofloxacin
   b. A seven-day course of cephalexin
   c. A 14-day course of nitrofurantoin
   d. A 14-day course of ampicillin

2. **Which of the following is a true statement about antibiotic treatment of pyelonephritis as described by Talan and colleagues in their recent paper on uncomplicated pyelonephritis in women?**
   a. Resistance to ciprofloxacin was higher in the eastern United States.
   b. Resistance to trimethoprim-sulfamethoxazole was higher in the western United States.
   c. Resistances to ciprofloxacin and trimethoprim-sulfamethoxazole were decreasing over time.
   d. Resistance to trimethoprim-sulfamethoxazole was higher in the eastern United States.

3. **Because of the risk of adverse reactions, ketamine should be avoided in:**
   a. infants.
   b. women of childbearing age.
   c. young adults with a family history of schizophrenia.
   d. older adults with a history of coronary artery disease.

4. **Which of the following variables was found to independently predict inappropriate discharge from the ED with an acute coronary syndrome?**
   a. African-American race
   b. Age > 55
   c. Chief complaint of shortness of breath
   d. Left bundle branch block on the ECG

5. **Which of the following fluoroquinolones has been most significantly linked with phototoxicity?**
   a. Grepafloxacin
   b. Levofloxacin
   c. Trovafloxacin
   d. Sparfloxacin

6. **Which of the following has been linked to fluoroquinolone therapy?**
   a. Tendonopathy
   b. Osteogenesis imperfecta
   c. Chondromalacia patellae
   d. Osteoporosis

7. **Which of the following agents should *not* be co-administered with gatifloxacin, moxifloxacin, or sparfloxacin due to concerns about QT prolongation?**
   a. Ranitidine
   b. Theophylline
   c. Procainamide
   d. Metoprolol

T Wave Inversion After PSVT Conversion

By Ken Grauer, MD

Clinical Scenario: The ECG shown in the Figure was obtained from a previously healthy 42-year-old man who presented to the emergency department in PSVT at a rate of just under 150 beats/minute (follow-up tracing to last month's *ECG Review*). The patient had been experiencing atypical chest discomfort that completely resolved after treatment of his arrhythmia. The ECG shown was recorded 10 minutes after conversion to normal sinus rhythm. Should this patient be admitted to the hospital to rule out acute infarction?

Interpretation: As noted above, the patient now has converted to normal sinus rhythm, as evidenced by regular upright P waves in lead II. The most remarkable finding on this tracing is the presence of fairly deep, symmetric T wave inversion in the inferior and lateral precordial leads. The point to emphasize is that other than ischemia, this T wave inversion most probably represents the "post-tachycardia" syndrome, in which transient T wave inversion (lasting hours or more) may be seen without necessarily reflecting coronary ischemia. Whether to admit this patient should depend on the clinical situation (i.e., not necessarily needed if symptoms have completely resolved and the patient is an otherwise healthy young adult without any evidence of underlying heart disease). Bonus—this post-tachycardia tracing confirms that the terminal negative notching of the QRS complex in the inferior leads and the terminal r' in lead V_1 of last month's *ECG Review* tracing was in fact the result of retrograde atrial activity during the reentry tachycardia. ❖

In Future Issues:

Diagnostic Imaging in Appendicitis