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B-type Natriuretic Peptide Useful Marker in Diagnosing CHF

ABSTRACT & COMMENTARY

Source: Maisel AS, et al. Rapid measurement of B-type natriuretic peptide in the emergency diagnosis of heart failure. *N Engl J Med* 2002;347:161-167.

ACUTE CONGESTIVE HEART FAILURE (CHF) OFTEN IS DIFFICULT to differentiate from other cardiac and non-cardiac causes of dyspnea in patients presenting to the emergency department (ED). B-type natriuretic peptide (BNP) is a neuro-hormone natriuretic polypeptide secreted by cardiac ventricular tissue in response to ventricular volume expansion and pressure overload. Recent studies suggest that serum BNP levels increase with acute CHF exacerbations and may aid in the diagnosis in the emergent setting.

In this study, the authors performed a multi-center, international (five United States and two European sites), prospective study investigating the predictive value of serum BNP levels measured by a fluorescence immunoassay rapid bedside kit (Triage, Biosite) for the diagnosis of acute CHF in patients with acute shortness of breath. Two independent cardiologists (blinded to BNP results) reviewed all ED and hospital records after patient discharge to determine a final diagnosis of either dyspnea due to acute CHF, dyspnea due to non-cardiac causes in patients with left ventricular (LV) dysfunction, or dyspnea not due to CHF.

Of the 1586 patients enrolled in the study, 744 (47%) were diagnosed with acute CHF, 72 (5%) with non-cardiac dyspnea with LV dysfunction, and 770 (49%) with no finding of CHF. Serum BNP levels were significantly higher in the acute CHF group (675 pg/mL ± 450 SD) when compared to either the LV dysfunction group (346 pg/mL ± 390) or no CHF group (110 pg/mL ± 225).

Moreover, among patients with CHF, higher BNP levels correlated with increased severity. Mean BNP levels for acute CHF patients with NYHA class I severity were 244 pg/mL (± 286), but increased to 389 pg/mL (± 374) in those with class II, 640 pg/mL (± 447) in those with class III, and 817 pg/mL (± 435) in those with class IV severity.

The authors conclude that the rapid, bedside measurement of BNP is useful in conjunction with other clinical information in establishing

INSIDE

or excluding the diagnosis of CHF in patients presenting with acute dyspnea to the ED.

COMMENTARY BY THEODORE C. CHAN, MD, FACEP

In this industry-sponsored study, a rapid, point-of-care BNP assay demonstrated excellent utility in discriminating CHF from other causes of dyspnea in patients presenting to the ED. Moreover, BNP levels correlated with overall severity in CHF patients.

BNP secretion from cardiac ventricular tissue is part of a cascade of neuro-hormonal responses to LV dysfunction, volume expansion and pressure overload. Other investigators have reported that BNP, in combination with troponin and c-reactive protein (CRP), each may provide important prognostic value and serve as a new "multi-marker" approach to cardiac acute coronary syndrome (ACS) patients.[1]

Natriuretic peptides such as BNP represent a favorable side of neurohormonal activation as their diuretic, natriuretic, and vasodilator properties aim to improve the loading conditions on the failing heart. Indeed, recent research on a therapeutic BNP medication (nesiritide) has shown promise in the treatment of severe CHF.[2]

In interpreting the results of this study on the utility of the bedside BNP assay, it is important to note that the investigators excluded patients with acute myocardial infarction, as well as renal failure. Moreover, BNP levels demonstrated a large variance in all three groups (acute CHF, LV dysfunction, and no CHF) as demonstrated by the sizeable standard deviations. It is notable that the BNP cutoff level with the highest diagnostic accuracy (100 pg/mL) was actually lower than the mean BNP level in the no CHF group (110 pg/mL). Thus, while BNP levels have clear diagnostic utility, they certainly are not infallible, and must be used in conjunction with other pertinent clinical findings in these patients. ❖

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Effectiveness of OTC Cough Medications Doubtful, at Best

ABSTRACT & COMMENTARY

Source: Schroeder K, et al. Systematic review of randomised controlled trials of over-the-counter cough medicine for acute cough in adults. *BMJ* 2002;324:329-331.

THIS COCHRANE SYSTEMATIC REVIEW EXAMINED ALL randomized controlled trials published through the year 2000. Studies were included if the participants were adults with cough fewer than three weeks' duration, the intervention evaluated was administration of an over-the-counter (OTC) cough preparation, and the frequency or duration of cough was a reported outcome. Studies were excluded if the participants had a chronic cough or underlying lung disease, or if non-conventional therapies were evaluated.

The authors identified only 15 studies meeting these criteria. The number of studies examining each specific type of cough preparation ranged from one to five. Outcomes were measured in different ways, and the overall

quality of the studies was not high. The few available studies were split on whether there was any benefit to either dextromethorphan or codeine as antitussives. There was no clear benefit to guaifenesin (as an expectorant) or to antihistamine-decongestant combinations. A handful of drug combination trials also yielded mixed and underwhelming results. The authors conclude that there is no clear evidence that OTC cough preparations are helpful in acute cough, and therefore none of the drugs can be recommended without qualification.

COMMENTARY BY DAVID J. KARRAS, MD, FAAEM, FACEP

It is somewhat surprising that there is so little evidence supporting the use of OTC cough preparations. As with many medications that have been available for decades, it is likely that many of these drugs never would have been approved for cough treatment if they were applying to the U.S. Food and Drug Administration today. The Cochrane collaborators have pooled the collective fund of knowledge regarding the utility of these medications and have found the evidence supporting their use to be highly limited, if not absent entirely.

There are a number of potential limitations to this type of study. Where there is conflicting evidence from several studies, it is difficult to determine which study should be regarded as more definitive (although we are told all the trials meet fairly stringent criteria). The number of trials examining each specific medication was very small and may not lend itself to pooling of data in the manner of this review. Apparently, codeine is available as an OTC medication in the United Kingdom, and we are not told whether the dose is equivalent to that prescribed for cough in the United States. Despite these considerations, the study provides an important counterpoint to the number of expert reviews advising OTC cough preparations as first-line therapy for adults with acute cough. ❖

New Technology Provides Rapid Laboratory Turnaround

ABSTRACT & COMMENTARY

Source: Mainor BH, et al. Evaluation of a portable clinical analyzer in the pediatric emergency department: Analysis of cost and turnaround time. *South Med J* 2002;95:634-638.

Recent advances in point-of-care testing have shown promise in reducing turnaround time in adult emergency departments (EDs). Now, Mainor and colleagues present data on the impact of a handheld portable clinical analyzer (PCA) evaluated in the pediatric ED.

The researchers enrolled 20 patients, from birth to age 16, who were seen at Children's Hospital of Alabama in Birmingham. Each child had clinical indicators of serious illness warranting laboratory evaluation. Diagnoses included volume contraction (six cases), altered mental status with or without trauma (five cases), diabetic ketoacidosis (DKA) (three cases), seizure (three cases), congenital heart disease with respiratory distress (two cases), and possible sepsis (one case). Whole blood samples were processed utilizing the i-STAT PCA, a 21x6x5-cm battery-powered device weighing 520g. Individual chemical tests were determined by disposable cartridges containing calibrated biosensors standardized for 12 tests per cartridge. The range of tests included sodium, potassium, chloride, bicarbonate, glucose, blood urea nitrogen (BUN), pH, $pC0_2$, $p0_2$, oxygen saturation, ionized calcium, and hemoglobin. All PCA tests conducted by ED personnel were run parallel to samples submitted simultaneously to the central hospital laboratory.

The average turnaround time for PCA testing was 2.2 minutes, compared to the central laboratory time of 56.3 minutes, for an average time difference of 54.2 minutes ($p < 0.001$; 95% CI -44.12 to -64.25 min). Average PCA cost was $9 per cartridge vs. hospital laboratory cost of $10.65 per test grouping, for a mean difference of $1.65 ($p = 0.02$). Average blood volume required for PCA testing was 0.29 mL, vs. 2.62 mL for standard laboratory analysis, for a difference of 2.32 mL ($p < 0.001$, 95% CI -1.66 to -2.96 mL). The authors conclude that the i-STAT PCA employed in the pediatric ED generated results significantly faster than the central laboratory.

COMMENTARY BY MICHAEL FELZ, MD

The handheld device was less expensive to operate and required significantly less whole blood per patient. This study captured my attention for several reasons. First, the idea of point-of-care testing, with results available within two minutes of phlebotomy or finger stick, is quite appealing for faster decisions and earlier intervention at the bedside of ill children. What a boon to management it would be to have evidence for volume contraction, or DKA, or hypercarbia in fewer than five minutes, and with only 1/3 mL of blood. The authors comment that they even utilized failed IV access or a "blown" vein to obtain enough blood for handheld cartridge analysis.

Second, the application of PCA methodology could eliminate many hassles, including staff required to draw, handle, and transport blood vials; excess demand on already stressed laboratory technologists; and erratic phone or electronic relay of lab results to physicians. Third, parents of ill children would marvel at the ease of obtaining a mere 0.3 mL of blood (by fingerstick, not venipuncture),

and the revolutionary concept that results take only two minutes—even at midnight in a crowded ED. Fourth, I foresee more incisive decision-making, more rapid and specific intervention, and enhanced patient flow, all of which would benefit patients in rooms as well as those waiting to be seen. Finally, it seems to me that administrators monitoring health care expenses would view i-STAT performance capability as a promising investment in hospital cost containment.

I recommend that we stay tuned for expanded studies of PCAs on the horizon. One of my adult ED colleagues carries an i-STAT in his pocket, persuaded that it makes him a finer physician. And so, for my money, in evaluation of the sick child requiring analysis of electrolytes, fluid balance, or blood gases in the ED, the user-friendly handheld PCA wins—hands down. ❖

Special Feature

Thrombolytic Therapy for Pulmonary Embolism

By Esther Chen, MD, and Stephanie B. Abbuhl, MD

Most relevant to the emergency care of patients with pulmonary embolism (PE) is rapid diagnosis with risk stratification and initiation of appropriate therapy, with the goals of reducing mortality and improving clinical outcome. Despite improvements in the diagnosis and treatment over the past 30 years, PE still causes approximately 9% of in-hospital deaths and may represent up to 36% of unexplained cardiac arrests with pulseless electrical activity.[1,2] In one prospective study of consecutive emergency department (ED) patients who presented with pleuritic chest pain, 21% were found to have PE as diagnosed on pulmonary angiogram or autopsy.[3] One of the primary determinants of mortality from PE is right ventricular dysfunction (RVD) causing circulatory collapse and shock, resulting in a mortality rate of 59%.[4] The use of thrombolytic therapy (TT) has been suggested in these patients, where the immediate goals are to normalize pulmonary vascular resistance, prevent recurrent embolism, and improve survival.[5] The indications for TT remain controversial. Faced with the challenges of rapid decision-making, the ED physician quickly must determine the correct diagnosis and consider the use of TT along with other treatment options, while balancing the potential risks and benefits of therapy.

Pathophysiology of PE

The pulmonary circulation has a remarkable ability to accommodate small to moderate-sized blood clots because of its redundant vasculature. This excess in pulmonary vessels is necessary to accommodate the normal increase in blood flow that occurs during exercise. It is this reserve that allows post-pneumonectomy patients to maintain their ventilation/perfusion (V/Q) balance by opening up vascular beds in the unresected lung.[6] This is also the reason why healthy patients with no underlying lung disease can have multiple PEs and present with little or no change in their pulse rate, respiratory rate, $p0_2$, or A-a gradient.[7]

As clot burden increases, however, there is a limit to the lung's ability to compensate for obliterated lung vessels, and pulmonary vascular resistance rises. The release of vasoactive substances such as serotonin and bradykinin can cause local bronchial constriction and pulmonary vascular redistribution. With increasing resistance, the right ventricle loses its capacity to increase stroke volume and becomes overloaded and dilated, leading to right heart failure with hemodynamic compromise. Major PEs almost always are associated with hypoxemia from the large areas of pulmonary deadspace and significant V/Q mismatch. In addition, the remaining limited areas of intact pulmonary perfusion are forced to accommodate the entire cardiac output and are overperfused, effectively creating a shunt.[6]

Mechanism of Action of Thrombolytic Agents

Effective pharmacologic regimens for the treatment of PE fall into two categories: drugs that inhibit coagulation (heparin, low molecular weight heparin, warfarin) and direct thrombolytic agents (streptokinase, urokinase, and tissue plasminogen activator [tPA]). Heparin exerts its effect by activating antithrombin III, which in turn inhibits thrombin, preventing further fibrin deposition on the thrombus. With clot stabilization, heparin enables the patient's endogenous fibrinolytic mechanisms to take effect, but heparin itself does not lyse existing clot. This concept has been termed "secondary prevention" and is distinctly different from the "primary therapy" of TT and embolectomy.[8]

Thrombolytic agents dissolve thrombi by activating plasminogen to plasmin, which degrades fibrin to soluble peptides.[9] The theoretic advantages of TT over anticoagulation are threefold. First, there should be rapid and complete clot lysis, leading to improvements in hemodynamics, gas exchange, and mortality; second, thrombolysis should dissolve the original venous thrombosis and reduce the risk of recurrent venous thromboembolism; third, the risk of chronic pulmonary hypertension and chronic venous stasis complications should be reduced.[10] The TT agents approved for use in PE are streptokinase, urokinase, and tissue plasminogen activator (alteplase, tPA), although there have been several trials with others, such as reteplase and saruplase. In the few comparison studies, there have been no statistical differences in efficacy or safety among the approved agents.[10]

Evidence Comparing TT with Anticoagulation

In several small, randomized trials and in the larger Urokinase Pulmonary Embolism Trial (UPET), undifferentiated patients with PE were prospectively studied, comparing the effects of thrombolytic agents followed by heparin with heparin alone.[11,12,13] These studies have been systematically reviewed in an excellent article by Arcasoy and Kreit.[10] In general, these studies concluded that TT significantly increased pulmonary blood flow and improved hemodynamics in the immediate post-treatment period. However, between two hours to seven days, depending on the design of the trial, these differences disappeared. None of these studies revealed a significant difference in mortality or recurrent PE between the two groups. It was not clear if there was truly no difference, or if larger studies would reveal a difference in outcome.

A study by Goldhaber in 1993 was one of the first to suggest that important advantages to TT may exist.[14] A total of 101 hemodynamically stable patients were randomized to receive either heparin or tPA and evaluated for right ventricular (RV) function by echocardiogram at baseline, three, and 24 hours. Pulmonary blood flow was measured by perfusion scan at baseline and at 24 hours. The patients who received tPA showed significantly greater improvements in RV function and pulmonary perfusion than the heparinized group. The improvement in RV function was greatest in patients with baseline RVD (89% improvement in the tPA group vs 44% in the heparin alone group; $p = 0.03$). No patient in the tPA group had a recurrent PE at 14 days, compared to a 9% clinically suspected recurrence rate (two fatal and three non-fatal) in the heparin group, although this did not reach statistical significance ($p = 0.06$). All recurrences occurred in patients with RVD. Despite showing hemodynamic improvement with TT, this study was not powered to evaluate a survival advantage.

A similar improvement in cardio-pulmonary function in TT-treated patients was reported by Dalla-Volta et al in 1992.[15] Thirty-six hemodynamically stable patients with PE were assigned to either alteplase ($n = 20$) or heparin ($n = 16$). Improvements in vascular obstruction and pulmonary artery pressures were significantly greater in the TT group vs. the heparin group at two hours post-treatment. However, there were no differences between the two groups when comparing follow-up lung scans done on days seven and 30. Major bleeding episodes occurred in 15% of the alteplase group and in 12.5% of the heparin group.

The first randomized trial to show a decrease in mortality using TT involved only eight patients with major PE and shock who were randomized to receive either TT (bolus streptokinase) or heparin.[16] All patients in the heparin group died, whereas all patients who received TT survived. On postmortum examination, all three patients who were autopsied died of RV infarct. This study originally was designed to include 40 patients, but was prematurely terminated because of the significant survival advantage shown with TT. While the study has been criticized for a longer time delay from onset of symptoms to treatment in the heparin group, the results are impressive.

Konstantinides et al published a study from the MAPPET registry that provided insight into the use of TT in patients with RVD, but without shock.[17] In the subgroup of 719 patients with moderate or severe RVD and normal systemic blood pressure, the group that received TT had a significantly lower mortality at 30 days when compared to the heparin group (4.7% vs 11.1%). Patients treated with TT also had significantly less frequent recurrent PE than the heparin alone group (7.7% vs 18.7%). Major bleeding complications were significantly higher in the TT group (21.9% vs 7.8%), but cerebral hemorrhage occurred in only two patients in each group. The major limitation of this study was its non-randomized design and inevitable selection bias, in that older patients with underlying co-morbid conditions were selected to receive heparin instead of TT.

Risk Stratification

Along with basic clinical parameters, echocardiography has emerged as a key tool in determining the risk of adverse outcomes in patients with PE. Abnormalities on transthoracic echo (TTE) that predict a large PE include right ventricular dilatation and hypokinesis, paradoxical motion of the interventricular septum with septal flattening, tricuspid regurgitation, and lack of collapse of the inferior vena cava during inspiration.[18] Studies that have attempted to define the relationship between RVD and the size of the PE have found that approximately 30% of non-perfused lung predicts most patients with right ventricular hypokinesis.[18] While TTE rarely will show actual thrombus, transesophageal echo (TEE) often can directly visualize the extent of the thrombus and its accessibility for surgical embolectomy. However, TEE is limited by the expertise required, the conscious sedation needed, and the fact that a left pulmonary artery embolism can be obscured by the left main bronchus.

Several studies reliably have established RVD on transthoracic echo as a predictor of mortality from PE.[14,17,19,20,21,22] In the Konstantinides study, the overall 30-day mortality in patients with RVD and those with normal RV function was 10% and 4.1% ($p = 0.018$), respectively.[17] In another MAPPET registry study, Kasper et al reported 1001 consecutive patients with acute PE who were divided into four groups: 1) RVD or pulmonary HTN on echo without arterial hypotension, 2) arterial

hypotension without shock, 3) arterial hypotension with shock, 4) cardiogenic shock requiring CPR.[19] The overall mortality was 22%, but highest in group 4 (65% vs 8.1% in group 1). In a second study by Kasper et al, 317 patients studied echocardiographically were subsequently divided into two groups, either with RVD (n = 87) or without RVD (n = 230).[20] Patients with RVD had a significantly higher mortality than those without (19% vs 5.7%).

Most recently, in a study by Grifoni et al, 209 patients diagnosed with acute PE by either high probability pulmonary perfusion scan, positive CT scan, or pulmonary angiogram were categorized into four groups: 1) patients with shock or cardiac arrest, 2) hypotensive patients without shock, 3) patients with RVD but normotensive, 4) patients without RVD.[22] PE-related mortality was 32% in patients with shock, 5% in normotensive patients with RVD, and 0% in patients without RVD.[15]

Complications of Thrombolysis

The most important complication of TT is hemorrhage, and the risk of significant bleeding must be carefully weighed against the potential benefits. In contemporary studies the outcome of "major hemorrhage" often is defined as including fatal, intracranial, and/or bleeding requiring surgery or transfusion.[10] Given this definition, the average incidence of major hemorrhage is 6.3% with TT and 1.8% with heparin, although the range is wide and depends on numerous patient factors, including age, comorbidities, and presence of hyper- and hypotension.[10] The frequency of major bleeding complications has been as high as 15-27% in some studies.[13,15] The rates often are higher in older studies where venous cutdowns routinely were done for angiography and when transfusions were given more readily. In a review of pooled data, the overall incidence of intracranial hemorrhage was found to be 1.2%, with fatal bleeding in about half of these patients.[10]

Intrapulmonary Thrombolysis

Potential advantages of intrapulmonary over systemic thrombolysis are three-fold. First, local delivery of TT may lead to more rapid and complete clot lysis; second, delivery of the medication directly near the clot may require a smaller amount of the drug to achieve the same result; third, if lower doses are used, there may be an associated lower risk of bleeding.[10] There is evidence from the interventional radiology literature that intrapulmonary administration of TT with or without mechanical fragmentation is successful in treating PE; however, these are mainly small case series.[23] Verstraete et al published a small pilot study that enrolled 34 patients with angiographically diagnosed PE who were randomized to receive systemic tPA (n = 15) or intrapulmonary tPA (n = 19).[24] A post-infusion angiogram showed a decrease in clot burden by 38% from baseline in both groups. There was no significant benefit of intrapulmonary over systemic TT administration. Furthermore, there was no difference in bleeding complications.

In addition to the small size, a significant criticism of the study by Verstraete et al is that the technique that was studied is no longer the standard of care. Intrapulmonary thrombolysis now almost always is coupled with mechanical fragmentation, which is thought to accelerate clot lysis due to the increase in surface area from the fragmentation of the clot. To our knowledge, there have been no randomized trials comparing this new technique with systemic fibrinolysis.[23]

Conclusion

Three risk stratification categories emerge to assist in acute decision making for the potential use of TT in PE patients:

- In patients with circulatory collapse or shock secondary to PE, TT appears to decrease mortality and recurrence rate as compared to heparin alone;
- In normotensive patients without evidence of RVD on echocardiogram, TT confers no benefit over anticoagulation;
- In normotensive patients with evidence of RVD but without shock, TT *may* decrease mortality and recurrent PE as compared to heparin alone. A careful assessment of the potential risks and benefits must be made on an individual basis. Furthrer randomized trials are needed to better assess the outcomes measures of both short- and long-term mortality with TT as compared to heparin alone. ❖

(Dr. Chen is Assistant Professor of Emergency Medicine, University of Pennsylvania School of Medicine, Philadelphia.)

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CME Objectives

To help physicians:

- Summarize the most recent significant emergency medicine-related studies;
- Discuss up-to-date information on all aspects of emergency medicine, including new drugs, techniques, equipment, trials, studies, books, teaching aids, and other information pertinent to emergency department care; and
- Evaluate the credibility of published data and recommendations.

Physician CME Questions

28. In the study by Maisel et al, B-type natriuretic peptide levels were the highest in patients with:
a. left ventricular dysfunction and non-cardiac dyspnea.
b. NYHA class IV heart failure.
c. acute myocardial infarction.
d. chronic obstructive pulmonary disease.

29. In healthy patients with acute cough, the literature clearly shows symptomatic benefit from:
a. empiric use of macrolide antibiotics.
b. use of over-the-counter antihistamines.
c. use of guaifenesin.
d. None of the above

30. For acute cough, over-the-counter cough remedies appear to be:
a. useless.
b. useful only if used in combination with antibiotics.
c. highly efficacious.
d. of unproven clinical benefit.

31. In the pediatric ED, the handheld portable clinical analyzer has been shown to:
a. document gram negative bacteremia.
b. eliminate the need for toxicology studies.
c. shorten turnaround time for chemistry results by nearly one hour.
d. enhance the likelihood of recovery from cardiac arrest.

32. Which of the following statements is false concerning the use of thrombolytic therapy (TT) for patients with pulmonary embolism?
a. There is definitive evidence to conclude that TT significantly improves pulmonary blood flow and improves right ventricular function in the immediate post-treatment period when compared to heparin alone.
b. There is no conclusive evidence to support the use of TT in stable patients with no RVD on echocardiogram.
c. There is evidence to support the use of TT in patients with PE and shock.
d. Recent studies have shown a similar rate of major bleeding episodes when comparing TT with heparin alone.

Digoxin Use in this 81-Year-Old Man?

By Ken Grauer, MD

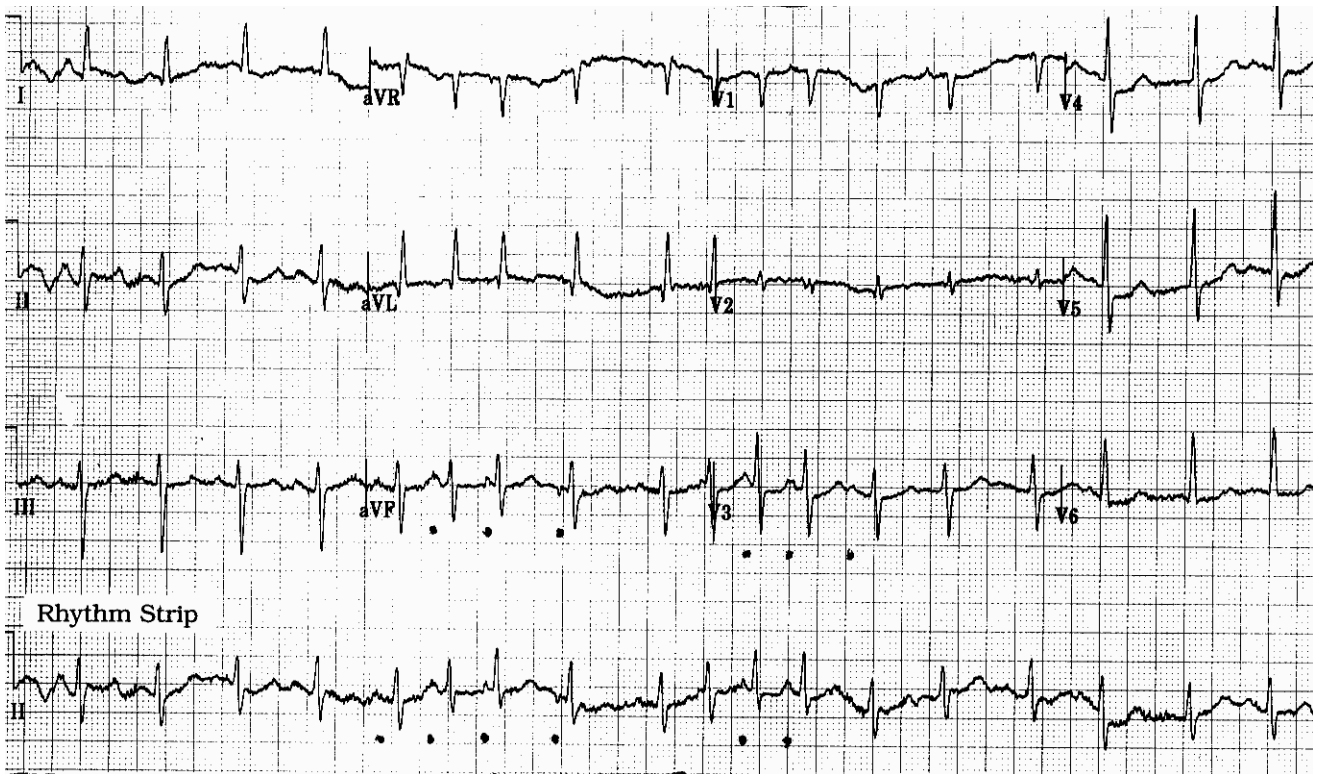

Figure. 12-lead ECG obtained from an 81-year-old man on digoxin.

Clinical Scenario: The ECG shown in the Figure was obtained from an 81-year-old man who presented with heart failure and pneumonia. Digoxin was among his many medications. Why do you suppose he was on digoxin?

Interpretation: Interpretation of the ECG in the Figure is made difficult by the presence of artifact in the baseline. One might be tempted to assume that the irregularly irregular rhythm seen in the lead II rhythm strip at the bottom of this tracing reflects atrial fibrillation. However, close inspection of the rhythm strip suggests that despite baseline wander and artifactual markings, there probably *is* atrial activity in this lead II rhythm strip. Directing one's attention to the deflections occurring just above the dots in the rhythm strip suggests the presence of *different* shaped P waves with varying PR intervals. That these deflections are likely to be real and true manifestations of atrial activity rather than artifact is suggested by confirmation in other simultaneously recorded leads of the presence of P waves. (*See dots in leads aVF and V_3.*)

Thus, this is an irregularly irregular supraventricular (narrow-complex) rhythm with multiple differently shaped P waves—a description that strongly suggests multifocal atrial tachycardia (MAT) as the etiology of the rhythm.

MAT most often occurs in the setting of chronic pulmonary disease. It is also sometimes seen in the presence of multisystem disease (such as pneumonia, sepsis, acid-base disturbance, or electrolyte disorders). The treatment of choice is to identify and correct the underlying medical cause(s) of the rhythm. One wonders if this 81-year-old man with heart failure mistakenly may have been placed on digoxin for heart failure and misdiagnosis of his irregular rhythm as atrial fibrillation. ❖

In Future Issues: **Pharmaceutical Industry Influence on Practice Guidelines**