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Inappropriate Drug Use in Older Persons

ABSTRACT & COMMENTARY

Synopsis: *Drug use in persons older than age 80 with dementia showed drug duplication and potent anticholinergic hazards, while nondemented elderly were mostly exposed to cardiovascular drugs that could aggravate their underlying diseases.*

Source: Giron MS, et al. *J Am Geriatr Soc.* 2001;49:277-283.

As part of an ongoing population study in Sweden, all individuals born in 1912 or earlier living in a certain district were invited to participate in this study, and 1810 enrolled (76% of eligible residents). Women made up 78% of the sample, and 13% resided in institutions. Dementia was established with both the MMSE exam and clinical confirmation when the study began in 1987-1989, with reassessment on all participants every 3 years. Drug data were collected during the follow-up in 1994-1996 through interviews and collection of the actual drug containers.

The mean number of drugs used in the overall sample was 4.6, with a range of 0 to 21. This rose to 4.8 drugs for those aged 90 and older who were not demented, and to 5.8 for that age who were demented. Less than 8% of any of these age groups used no drugs at all, and for institutionalized persons 100% fully used a mean number of 7 drugs.

The most commonly reported drugs used by both demented and nondemented groups were diuretics (39% and 30%), followed by analgesics (27% and 30%). Laxatives were next for demented elderly (28%), but only 13% for nondemented. Hypnotics and sedatives followed in high use for both groups.

Anticholinergic properties were found in 13% of drugs used by demented elderly, most often antipsychotics of low potency, and this group also had the most duplication of more than 1 drug from the same therapeutic/pharmacological class. Duplicate laxative drugs were found in 9% of demented elderly, who also had duplicate anxiolytics to use as needed in 3% of their drugs.

The most common potential drug-drug interactions found were in the use of digoxin with furosemide, where no potassium supplements were used in 69% of demented and 52% of nondemented cases.

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Another potential problem for 3% of demented elderly was the use of antidepressants and antipsychotics together.

The most common drug-disease interactions involved congestive heart failure, where beta-blockers were used in 12% of nondemented elderly. For patients with peptic ulcer disease, 27% were using systemic glucocorticoids, 18% aspirin, and 9% NSAIDs. For both groups, anticholinergic drugs were commonly used with BPH (14% of nondemented and 29% of demented elderly).

Finally, the average daily drug doses used were compared to maintenance recommendations, and found to be lower in 87% of demented and 75% of nondemented elderly. Only 13% and 18%, respectively, had daily doses exceeding recommendations.

■ COMMENT BY MARY ELINA FERRIS, MD

In this population study of older persons with and without dementia, Giron and colleagues found several

problems with physician prescribing. Giron et al claim that it is the first published study to evaluate appropriate drug use in this “very old” population, although similar studies have been published for elderly community-dwelling and nursing home residents. Consistent with those previous studies, potentially inappropriate medications were found in double-digit percentages, suggesting poor quality of health care for the elderly.^{1,2}

However, a closer look at the potentially inappropriate categories reveals the weakness of the allegations. Who would be surprised that vital antipsychotic medications have anticholinergic effects? Or that demented male patients older than 80 with BPH would still be prescribed such medications to control behavioral problems? Particularly in these frail older ages, the risks and benefits of any therapy must be balanced for the best effect. Furthermore, the use of multiple medications in a single category may indicate a complex problem rather than a deficiency in care.

The information does provide an interesting perspective on what medications patients are actually taking, since they obtained the data from the patients themselves and not from medical records. The number of drugs used was not surprisingly high (perhaps reflecting more about Sweden than the US), and the fact that lower doses were being prescribed reflects well on the geriatric skill of the practitioners, using the adage “start low and go slow” in prescribing for the elderly. The prevalence of potential disease-drug interactions, particularly with ulcers and ASA/NSAIDs, reminds us once again what has been shown in previous studies, that we need to ask our patients about all the multiple drugs they may be taking at home.³ ♦

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Association of Adult Celiac Disease with IBS

ABSTRACT & COMMENTARY

Synopsis: Irritable bowel syndrome patients (at least in the United Kingdom) should be routinely investigated for the presence of celiac disease.

Source: Sanders DS, et al. *Lancet.* 2001;358:1504-1508.

Irritable bowel syndrome (ibs) is extremely common in western populations. However, impor-

tant medical organizations such as the American Gastroenterological Association do not recommend any routine medical assessment of IBS patients. Three hundred consecutive new gastrointestinal patients at a University Hospital in Sheffield, England who fulfilled Rome II criteria for IBS were matched with 300 healthy controls. Consensus diagnostic criteria (Rome II criteria) for IBS include abdominal discomfort or pain with 2 of the following 3 features: discomfort relieved with defecation, onset associated with a change in frequency of stool, and onset associated with a change in form (appearance) of stool. Supporting symptoms of IBS include: fewer than 3 bowel movements/week, more than 3 bowel movements/day, hard or lumpy stools, loose (mushy) or watery stools, straining with stools, urgent stools, feeling of incomplete rectal emptying, mucus in stools, and abdominal fullness or swelling or bloating. All patients and controls in this study were evaluated for celiac disease using serum IgA antigliadin, IgG antigliadin, and endomysial antibodies (EMA). Positive antibody results were followed up with recommended duodenal biopsy. Sixty-six patients with IBS had positive antibody results, and 14 of these patients had celiac disease. Compared to matched controls, IBS was significantly associated with celiac disease ($P = 0.004$, odds ratio [OR] 7.0; 95% confidence interval [CI], 1.7-28.0). A variety of other medical problems were ultimately documented in many of the IBS patients including: 1 rectal cancer, 16 cases of diverticular disease, and 3 cases of inflammatory bowel disease (among other diagnoses).

■ **COMMENT BY MALCOLM ROBINSON, MD,
FACP, FACC**

Gluten sensitive enteropathy (celiac disease) is relatively common in England and elsewhere in the United Kingdom. Although these precise numerical results would not apply here in the United States, it is likely that we too may miss some patients with occult celiac disease who present with nondescript symptoms suggesting IBS. Use of the antibody testing as described in this article might well be appropriate in some individuals, especially if there are other findings suggesting celiac disease such as iron-deficiency anemia, diabetes, cryptogenic hyperamylasemia, peripheral neuropathy, and/or osteoporosis. Celiac disease is commonly thought to involve steatorrhea and weight loss, but some patients actually are quite constipated and without weight loss. Onset of celiac disease can be quite insidious. ❖

The Effect of Lowering Blood Pressure in Reducing the Risk for a Second Stroke

ABSTRACT & COMMENTARY

Synopsis: *A combination of the ACE-inhibitor perindopril and the diuretic indapamide lowered the risk of a second stroke in patients who had previously sustained a stroke or TIA.*

Source: Progress Collaborative Group. *Lancet*. 2001;358:1033-1041.

In recent years, the need to avoid treating hypertension in the setting of an acute stroke has been increasingly emphasized.¹ Only a few small, randomized trials have looked at lowering blood pressure after the period of acute illness to prevent future strokes, and results have been inconclusive.

The current study addresses this issue. A large group of physicians comprising the perindopril protection against recurrent stroke study (PROGRESS) collaborative group recruited 6105 patients in multiple countries. All had a history of prior stroke or transient ischemic attack ([TIA] 2 weeks to 5 years prior to enrollment). Forty-eight percent had hypertension, defined as systolic greater than 160 or diastolic greater than 90. Most were on antiplatelet therapy, and about half were taking antihypertensive therapy. Participants were randomized to receive perindopril (Aceon®) 4 mg daily or placebo. More than half of the patients receiving perindopril were also randomized to receive the diuretic indapamide at a dose of 2.5 mg daily. The main study end point was recurrent stroke.

Perindopril alone lowered blood pressure an average of 5/3 mm Hg, and had no effect on the incidence of recurrent stroke compared to placebo. By contrast, the combination of perindopril and indapamide lowered blood pressure an average of 12/5 mm Hg, and reduced the risk of recurrent stroke by 43% compared to placebo. The magnitude of blood pressure and stroke risk reduction in those receiving combination therapy was similar in hypertensive and nonhypertensive patients.

■ **COMMENT BY JOSEPH ZUCKERMAN, MD**

It's long been known that lowering blood pressure in hypertensive patients reduces the risk of a first stroke. This study suggests that reducing blood pressure in patients who've already had a stroke or TIA significantly reduces

the risk of a second stroke. This is useful information for clinicians, given the concern about lowering blood pressure in patients with known cerebrovascular disease.

The study also raises some interesting questions. First, are the benefits seen in the study related only to blood pressure lowering, or are the particular classes of medications used to lower blood pressure important? If the classes used are important, are there differences between different ACE-inhibitors? In the HOPE trial,² which used the ACE-inhibitor ramipril, there was an approximately 30% reduction in the risk of stroke in that high-risk group of patients, despite little effect on blood pressure. Second, are there some patients who should not be treated despite the results of this study? It would seem reasonable to avoid lowering blood pressure in patients with high-grade stenoses of major cerebral arteries, for example. Last, how aggressive should we be in treating patients who aren't hypertensive? While this study did not exclude patients based on initial blood pressure, it again seems prudent not to further lower blood pressure in patients who are already well within the normotensive range.

These questions will be answered by future studies. In the meantime, the main message of this study is that blood pressure reduction, as well as other standard treatment modalities such as antiplatelet and lipid-lowering agents, has a role in patients with cerebrovascular disease. ❖

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Dr. Zuckerman is Coordinator of Internal Medicine, Halifax Medical Center, Daytona Beach, Fla.

Effects of Inhaled Glucocorticoids on Bone Density in Premenopausal Women

ABSTRACT & COMMENTARY

Synopsis: *This study concludes that inhaled glucocorticoids lead to a dose-related loss of bone at the hip in premenopausal women.*

Source: Israel E, et al. *N Engl J Med.* 2001;345:941-947.

One hundred nine premenopausal women with the diagnosis of asthma, between 18 and 45 years

of age, were cohorted into 3 groups: those not taking inhaled glucocorticoids (n = 28); those taking 4-8 puffs per day of inhaled glucocorticoids (n = 39); and those taking more than 8 puffs per day (n = 42). No clinically relevant differences were seen among the 3 groups in weight, height, calcium intake, FEV₁, physical activity, smoking history, oral contraceptive use, bone-density, or biochemical values except for age, history of oral glucocorticoid therapy, and past or current use of topical inhaled glucocorticoids. Among the exclusion criteria were women who had received more than 2 short courses (lasting 2 weeks or less) of oral or parenteral glucocorticoids in the preceding year or any oral or parenteral glucocorticoids in the preceding 3 months.

At baseline, spirometry and bone density of the total hip, trochanter, femoral neck, and lumbar spine were performed with measurement of biochemical markers. Physical activity was assessed by a validated questionnaire. At subsequent visits at 6 months, 1, 2, and 3 years, information on medication use, diet and activities, measured bone density, and biochemical markers were reviewed and updated.

Israel and colleagues demonstrated a negative linear association between the average number of puffs per day of inhaled glucocorticoids and the yearly change in bone density at both the total hip and the trochanter ($P = 0.01$ and $P = 0.005$, respectively). Each additional daily puff of the inhaled glucocorticoid was associated with a decline in bone density of 0.00044 g per square centimeter per year at both sites, but there was no significant association with the degree of decline at the femoral neck and spine (-0.00005 and -0.00008 g per square centimeter per year per puff, respectively [$P = 0.85$ and $P = 0.68$, respectively]). This negative association was present even after adjustment for parental glucocorticoids, topical nasal glucocorticoids, and oral contraceptives. No correlation was found with urinary N-telopeptides, calcium, and cortisol values and serum osteocalcin, calcium, cortisol, and parathyroid hormones.

■ COMMENT BY DAVID OST, MD, & SYED RIZVI, MD

Inhaled glucocorticoids have become a key element in the maintenance treatment of bronchial asthma.¹ It is well known that long-term systemic steroids cause osteoporosis,² whereas inhaled glucocorticoids have been believed to avoid such side effects. The results of previous prospective and cross-sectional studies of the effects of inhaled glucocorticoids on bone loss have been inconsistent.³⁻⁶ These studies have been limited by small sample size, short duration, and presence of confounding factors such as intermittent use of systemic glucocorticoids, lack of

appropriate controls, superimposed menopausal bone loss, and differences among participants in the severity of asthma that might have affected physical activity.

In the present study, Israel et al were able to demonstrate a dose-related negative effect of inhaled glucocorticoids on bone density even among patients who did not receive systemic steroids and who had adequate intake of calcium and vitamin D. Furthermore, urinary and serum biochemical markers did not predict the extent of bone loss. ❖

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Pharmacology Update

Drotrecogin Alfa (Activated) (Xigris—Eli Lilly and Company)

By William T. Elliott, MD, FACP,
and James Chan, PharmD, PhD

The fda recently approved the first biologic treatment for severe sepsis. Drotrecogin alfa (activated), a glycoprotein serine protease produced by genetic engineering, has the same amino acid sequence as human plasma-derived Activated Protein C. It appears to have antithrombotic, anti-inflammatory, and profibrinolytic action in patients with sepsis. Drotrecogin alfa will be marketed by Lilly as Xigris.

Indications

Drotrecogin is indicated for the reduction of mortality in adult patients with sepsis associated with acute organ failure (ie, severe sepsis) who have a high risk of mortality.¹ In the clinical study, risk of mortality was determined by acute physiology and chronic health evaluation score (APACHE II).

Dosage

Drotrecogin should be infused intravenously at a rate of 24 µg/kg/h of a total of 96 hours.

It is supplied as 5 mg and 20 mg single-use vials. The lyophilized powder should be stored under refrigeration and protected from light.¹

Potential Advantages

In patients with systemic inflammation and organ failure due to acute infection, drotrecogin was associated with a absolute reduction in the risk of death of 6.1% (24.7% vs 30.8%) 28 days after the start of infusion.²

Potential Disadvantages

Bleeding is the most common adverse effect of drotrecogin. The incidence of serious bleeding (eg, intracranial hemorrhage, life-threatening bleeding) compared to placebo was 3.5% vs. 2.0%.² Patients at risk for bleeding should be evaluated on a risk to benefit basis. Drotrecogin is contraindicated in patients with active internal bleeding, recent hemorrhagic stroke or intracranial or intraspinal surgery, severe head trauma, other trauma associated with an increased risk of life-threatening bleeding, presence of an epidural catheter, or intracranial neoplasm, mass lesion, or evidence of cerebral herniation.¹

There is currently no evidence to suggest that patients with severe sepsis but with a lower risk of death would benefit from drotrecogin.¹

Comments

Sepsis is the systemic inflammatory response to infection. Severe sepsis is sepsis associated with organ dysfunction, hypoperfusion, or hypotension.^{3,4} The sequelae of sepsis are the result of interplay between the inflammatory cascade and the coagulation cascade. Protein C is one of the body's defenses against thrombosis. It possesses antithrombotic, anti-inflammatory, and profibrinolytic effects. Data indicate that protein C deficiency might be predictive of death associated with sepsis.⁵⁻⁷ The safety and efficacy of drotrecogin, which is a genetically engineered version of naturally occurring Activated Protein C, was demonstrated in Recombinant Human Activated Protein C Worldwide Evaluation in Severe Sepsis (PROWESS) trial and was the basis for the approval of the agent.² Patients were eligible for the trial if they had a known or suspected infection and the following criteria within a 24-hour period: 3 or more signs of systemic inflammation and sepsis-induced dysfunction of at least 1 organ or system that lasted no longer than 24 hours. Signs of systemic inflammation are

temperature $\geq 38^{\circ}\text{C}$ or $\leq 36^{\circ}\text{C}$, heart rate ≥ 90 bpm, respiratory rate ≥ 20 breaths/min or $\text{PaCO}_2 \leq 32$ mm Hg, or WBC count $\geq 12,000/\text{mm}^3$ or $\leq 4000/\text{mm}^3$ or $> 10\%$ immature neutrophils. Patients in the trial had an average APACHE II score of 25, more than 73% were on mechanical ventilation and more than 70% were in shock. Time to initiation of antibiotics was within 48 hours. Patients at risk for bleeding disorders, those not expected to survive 28 days, those treated with drugs such as heparin, anticoagulants, or antiplatelet agents, and others with suppressed immune systems were excluded. Eight hundred and forty (840) were assigned to placebo and 850 to drotrecogin (24 $\mu\text{g}/\text{kg}/\text{h} \times 96$ h). Baseline characteristics were generally comparable except there were more patients in the placebo groups on mechanical ventilation (77.6% vs 73.3%). Drotrecogin, administered no later than 24 hours after meeting study inclusion criteria resulted in an absolute reduction in risk of all-cause 28-day mortality of 6.1% (24.7% vs 30.8%, $P = 0.005$). Treatment with drotrecogin resulted in lower plasma D-dimer levels, and greater decreases in serum interleukin-6 levels, indicators of antithrombotic and anti-inflammatory activity, respectively. Those who received drotrecogin also appeared to have greater numbers of vasopressor and ventilator-free days.^{8,9} The results also suggest that patients with a greater number of organ failures had a greater absolute risk reduction in mortality, although the study was not sufficiently powered to distinguish these potential differences.⁹ Protein C levels may not be a predictor of drotrecogin success in this population. Serious bleeding was higher in the drotrecogin group compared to placebo (3.5% vs 2.0%, $P = 0.06$). Neutralizing antibodies against drotrecogin were not detected.

Drotrecogin is expensive with a wholesale cost of \$6800 per patient.

Clinical Implications

It is estimated that about 750,000 cases of severe sepsis occur each year in the United States with about a 30% mortality.¹⁰ The hospital cost is estimated at \$17 billion and more than \$22,000 per case. Drotrecogin alfa (activated) is the first agent approved to treat severe sepsis. Balancing the cost and benefit of this agent will be a challenge for decision makers. Based on the study results, 1 life would be saved for about every 16 patients treated with drotrecogin. This translates to about \$108,800 per life saved. If the PROWESS entry criteria are generally accepted, the number of treated patients could be substantial. Padkin et al indicated that 28% of all intensive care admissions met the criteria.¹¹

The role will ultimately be determined as clinicians gain broader experience. ❖

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CME Questions

43. For an elderly person with known peptic ulcer disease, which of the following medications should be used with caution?
 - a. NSAIDs
 - b. Glucocorticoids
 - c. Aspirin
 - d. All of the above
44. Irritable bowel syndrome may be associated with documented celiac disease, including the presence of antibodies to gliadin, in what percentage of patients in a recent United Kingdom study?
 - a. 39%
 - b. 75%
 - c. 5%
 - d. 25%
 - e. None of the above
45. Patients with a prior stroke or TIA who were treated with a combination of perindopril and indapamide, on average:
 - a. sustained a 5/3 mm Hg reduction in blood pressure and a 43% reduction in stroke risk.
 - b. sustained a 12/5 mm Hg reduction in blood pressure and no significant reduction in stroke risk.
 - c. sustained a 12/5 mm Hg reduction in blood pressure and a 43% reduction in stroke risk.
 - d. sustained a 5/3 mm Hg reduction in blood pressure and no significant reduction in stroke risk.
 - e. None of the above
46. All of the following have been used as "maintenance" treatment of bronchial asthma *except*:
 - a. inhaled corticosteroids.
 - b. leukotriene antagonist/inhibitors.
 - c. cromolyn sodium.
 - d. short-acting beta agonist.

By Louis Kuritzky, MD

Prevalence of Hereditary Hemochromatosis in Late-Onset Type 1 Diabetes Mellitus

It comes as a surprise to many clinicians that hemochromatosis (HCRM) is literally one of the most common genetic disorders in persons of northern European descent; in America, it has a gene frequency of 10%, hence it is more frequent than such disorders as cystic fibrosis. HCRM can manifest diversely, including liver disease, diabetes, heart failure, arthritis, and pituitary hypogonadism. Ellervik and colleagues postulated that HCRM is often overlooked as an etiology of, or contributor to, such disorders.

The study population included 716 type 1 adult-onset diabetics. Adult diabetics were chosen because systemic manifestations of HCRM usually manifest after age 50. The odds ratio (4.6) for homozygous HCRM in the diabetic population when compared to the unselected comparison population suggests a relevant role for HCRM in adult onset type 1 diabetes.

All patients who were HCRM homozygotes manifested an elevated serum transferrin saturation. Ellervik et al conclude that HCRM, a potentially correctable cause of diabetes and other maladies, is often overlooked. Their data suggest that, extrapolating from their Danish population, 15-20 cases of type 1 diabetes per million population could be prevented by discovery and appropriate treatment of HCRM with simple venesection. They further suggest that any type 1 adult onset diabetic merits screening for HCRM, since disease progress could be favorably affected by venesection control of HCRM. ❖

Ellervik C, et al. Lancet. 2001;358:1405-1409.

Hormone Replacement Therapy and Dry Eye Syndrome

Dry eye syndrome (des), also known as keratoconjunctivitis sicca, can cause substantial debilitation due to adverse symptoms of dryness and irritation, as well as the morbidity of increased risk of corneal infection, ultimately potentially leading to permanent visual impairment. Unfortunately, management tools for DES are often unsatisfactory.

The combination of estrogen and progesterone to menopausal women, hormone replacement therapy (HRT), is used by more than one third of American women, but the relationship between HRT and DES is not yet studied. Schaumberg and colleagues used the data set of the participants in the Women's Health Study (n = 39,876) to evaluate the relationship between HRT, estrogen replacement therapy (ERT), or non-use of hormone replacement with DES.

HRT use was significantly associated with DES. Estrogen replacement therapy (ERT) was associated with the highest prevalence of DES (9.1%), compared with HRT users (6.7%) and never-users of HRT (5.9%).

The mechanism(s) by which gonadal steroids might influence ocular lubrication is uncertain. Basic science studies have suggested that androgens favorably effect lacrimal and meibomian gland function, but estrogen may exacerbate dry eye. Schaumberg et al suggest that clinicians inform potential recipients of HRT/ERT that an increased likelihood of DES may be associated with its use. ❖

Schaumberg DA, et al. JAMA. 2001;286:2114-2119.

Association Between Myeloperoxidase Levels and Risk of Coronary Artery Disease

The association between inflammatory markers and the presence of atherosclerosis suggests that C-reactive protein, adhesion molecules, and other cytokines are potentially etiologically involved. Moreover, there is some substantiation for the use of such markers to predict risk of acute vascular events.

Myeloperoxidase (MPO) is an enzyme that is secreted from a variety of cells, such as neutrophils and macrophages. Normally, MPO is stored within quiescent cells, but is not released until the cells are activated, as occurs in states of acute inflammation. There is a putative link between MPO and endothelial dysfunction. Zhang and colleagues sought to establish the relationship between MPO activity and coronary artery disease. Study subjects included 333 adults, approximately half of whom had angiographically-demonstrated CAD.

MPO levels were significantly higher in persons with CAD than controls. Comparing levels of MPO, those in the highest quartile of MPO had almost a 9-fold increased odds ratio of CAD, compared with those in the lowest quartile. Zhang et al suggest that MPO levels may serve as a marker to identify persons with CAD who are not otherwise detected by typical risk factors. ❖

Zhang R, et al. JAMA. 2001;286:2136-2142.

1° AV Block in Lead V₁

By Ken Grauer, MD

Figure. 12-lead ECG obtained from an 87-year-old man who was thought to be in sinus tachycardia with 1° AV block.

Clinical Scenario: The 12-lead ECG shown in the Figure was obtained from an 87-year-old man, who was thought to be in sinus tachycardia with 1° AV block. Would you agree with this assessment of the rhythm?

Interpretation: The rhythm strip at the bottom of the tracing clearly shows the arrhythmia to be a regular supraventricular (*narrow-complex*) tachycardia at a rate of just under 120 beats/minute. It is tempting to say that the rhythm is sinus tachycardia with 1° (first degree) AV block, based on the presence of a seemingly prolonged “PR” interval in lead V₁. However, this is not the correct interpretation of this rhythm.

In general, 1° AV block is uncommonly seen in the presence of sinus tachycardia. On the contrary, much of the time when a prolonged PR interval is thought to be seen with a tachycardic rhythm, a mechanism *other than* sinus rhythm will be the cause of this finding. This is especially true when lead II fails to show a clearly defined upright P wave. Such is the case for the Figure shown here. Thus, a second clue that the mechanism of this rhythm is unlikely to be sinus is seen in lead II,

which shows no more than a poorly defined broadened and low amplitude positive deflection at the midpoint of the R-R interval. Although one cannot exclude the possibility that a sinus conducting P wave could be hidden within this low amplitude deflection, an alternative etiology for the rhythm is much more likely. Stepping back from the tracing provides the next clue—in the form of a subtle *sawtooth* pattern in the lead II rhythm strip (as well as in the other inferior leads). In further support of our theory that the rhythm in the Figure is atrial flutter is the ECG appearance in lead I, which shows a small rounded hump at the beginning of the ST segment, as well as an additional small rounded upright deflection preceding each QRS complex. Use of calipers allows one to walk out a consistent interval between each of these rounded deflections in lead I at a rate of 240/minute. Although the atrial rate of flutter activity in adults is most commonly closer to 300/minute, treatment with an antiarrhythmic drug may slow the atrial rate and produce flutter with 2:1 AV conduction at a ventricular rate of 120/minute as shown here. ❖