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Volume 1 Index Enclosed

# FAMILY PRACTICE ALERT™

*The essential monthly guide to developments in family medicine*

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## Cultures for Cellulitis

ABSTRACT & COMMENTARY

***Synopsis:*** *The method of obtaining a sample for culture from a focus of soft tissue infection was studied. Direct negative pressure aspiration resulted in significantly higher total protein recovery compared to the injection/aspiration method of first injecting 0.2 mL of sterile phosphate-buffered saline into the site followed by immediate aspiration. The direct aspiration method, without the injection of saline, yields higher amounts of aspirate material for culture.*

**Source:** Traylor KK, Todd JK. Needle aspirate culture method in soft tissue infections: Injection of saline vs. direct aspiration. *Pediatr Infect Dis J* 1998;17:840-841.

A bovine animal model of soft tissue infection was used to study aspiration through a skin nick with a 20-gauge needle attached to a syringe. Each of 12 pairs consisting of one sample taken by direct negative pressure aspiration and one sample by aspiration following injection of 0.2 mL of sterile phosphate-buffered saline was studied for total protein recovered. The difference was significantly higher (P = 0.019) for the direct aspiration method.

### COMMENT BY HAL B. JENSON, MD, FAAP

The best technique to culture cellulitis and soft tissue infections has been controversial. This study showed that direct aspiration, compared to injection/aspiration followed by aspiration, yields a greater amount of total tissue protein for culture. This is supported by a review of 13 published reports of the direct or injection methods that found a significantly higher recovery of bacteria with direct aspiration (75 of 160, 47%) than with the injection/aspiration method (77 of 403, 19%) (P < 0.001). This may be because the core material cut during needle aspiration is not subsequently ejected. One study has shown a higher rate of positive bacterial culture results with aspiration from the point of maximal inflammation than with aspiration from the leading edge,[1] although two subsequent studies have found both sites to be equivalent.[2,3]

Cultures of cellulitis are not always necessary. It is difficult for me to justify cultures of cellulitis on the face where even minimal scarring is undesirable, especially in patients prone to keloid for-



## INSIDE

mation. Even cases of periorbital cellulitis associated with minor trauma (e.g., insect bites, scratches) are almost always caused by *Staphylococcus* and/or *Streptococcus* rather than *Haemophilus influenzae* type b. This would be even more likely since the implementation of conjugate *H. influenzae* type b vaccines. Bringing a needle close to the eye in an uncooperative or anxious child for culture of periorbital cellulitis causes even more anxiety in me.

Another issue for children with cellulitis is the value of blood cultures. In immunocompetent children with uncomplicated cellulitis, blood cultures are almost always negative. In a cohort of 243 children with cellulitis, blood cultures were negative except in three children with varicella (who each grew group A-hemolytic streptococci) and two children with septic arthritis (one with *Streptococcus pneumonia* and one with *Staphylococcus aureus*).[4] It is unnecessary to obtain a blood culture in an immunocompetent child with uncomplicated cellulitis (acute onset of cellulitis associated with a break in the skin). (Please realize that this is hard for an infectious disease specialist to say, where the dictum is usually to culture early and often.) The appearance of cellulitis without a break in the skin as a portal of entry should suggest the possibility of extension of underlying infection (e.g., osteomyelitis or septic arthritis) and the need for further evaluation before beginning empiric treatment.

Cultures of tissues and blood from immunocompetent patients with uncomplicated cellulitis without unusual exposure to soil or fresh- or saltwater are generally unnecessary prior to the initiation of empiric antibiotic therapy for staphylococcal and streptococcal bacteria. When a culture of soft tissue or cellulitis is desired, this study supports the use of simple direct aspiration for optimal recovery of material for bacterial culture. Cultures of tissues and blood of patients with cellulitis are indicated for immunocompromised persons, those with development or progression of inflammation while on antibiotics, or with unusual exposures such as soil, fresh- or saltwater, or animal feces or products. ❖

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# Bundle Branch Block Revisited

ABSTRACT & COMMENTARY

***Synopsis:*** *Bundle branch block is a marker of a slowly progressive degenerative disease that affects the myocardium.*

**Source:** Eriksson P, et al. *Circulation* 1998;98: 2494-2500.

Conflicting data exist concerning the etiology and significance of bundle branch block (BBB) on the electrocardiogram (ECG). Thus, Eriksson and colleagues recorded 12-lead ECGs in a random sample of 855 men who were 50 years old in 1963 when they were recruited in the city of Goteborg, Sweden, and followed them for 30 years with periodic examinations. During the 30 years, 82 subjects with

BBB were found (10%). Most acquired BBB after entry; only 1% had BBB at entry. BBB became more prevalent with aging. At age 75 years, right BBB was four times more prevalent than left BBB (39 vs 9%). ECG evidence of left ventricular hypotrophy preceded left BBB in one-quarter of the subjects vs. 6% for right BBB. Risk factors for atherosclerosis, myocardial infarction (MI), and a diagnosis of ischemic heart disease were no different between those who developed BBB and those who did not. However, cardiomegally on chest x-ray ($P < 0.05$) and congestive heart failure (36% BBB vs 14% of controls; $P < 0.01$) were more common with BBB. Also, among those who died of cardiovascular causes, more subjects had a history of chronic heart failure with BBB (61%) vs. no BBB (28%; $P < 0.01$). Eriksson et al conclude that BBB is a marker of a slowly progressive degenerative disease that affects the myocardium.

### COMMENT BY MICHAEL H. CRAWFORD, MD

This study is consistent with the old adage that BBB is more commonly associated with cardiomyopathy rather than coronary artery diseases (CAD). In fact, no relation could be established between BBB and risk factors for atherosclerosis or overt CAD. This is consistent with other studies and the observation that BBB is not usually caused by acute MI. Also, the prevalence of BBB is highly correlated with advancing age, being 1% at age 50 and 17% at age 80 in men. Thus, CAD and BBB often coexist and this combination is known to increase mortality in acute MI and chronic CAD patients. Other studies suggest this may be due to a greater propensity to ventricular arrhythmias and sudden death, possibly due to prolonged repolarization. However, acute MI superimposed on a chronic progressive cardiomyopathy may result in a higher than expected mortality due to pump failure.

The major limitation of this study was that the small number of patients with BBB reduced the power for comparing left to right BBB, which many believe are of different significance. Also, ECGs were only recorded every 5-17 years, so details about the onset and potential causes of BBB are hard to decipher. In addition, there are few objective data about other cardiac diseases in this study. Nor are there electrophysiologic data about the site of block or the need for pacing. The implications of this study are that patients who develop or present with BBB should have an echocardiogram done to assess left ventricular function. The need for stress tests or coronary angiography is less clear in the absence of other indications for these procedures. ❖

# Atypical Glandular Cells of Undetermined Significance

ABSTRACT & COMMENTARY

***Synopsis:*** *Atypical glandular cells of undetermined significance on Pap smears were correlated with significant findings in 45% of patients.*

**Source:** Veljovich DS, et al. *Am J Obstet Gynecol* 1998; 179:382-390.

Veljovich and associates conducted a five-year retrospective review of screening cervical cytologic examinations diagnosed as atypical glandular cells of undetermined significance (AGCUS) to ascertain the types and frequency of pathologic conditions associated with this diagnosis. Three hundred forty-five evaluable patients were identified. The incidence of AGCUS was 0.53%. Pathologic findings for the respective Pap smears with the diagnosis of AGCUS—not otherwise specified—favor benign, squamous intraepithelial lesions, and favor neoplasia through the follow-up interval were as follows: squamous intraepithelial lesions in 11%, 8%, 38%, and 20%; adenocarcinoma in situ in 3%, 0%, 0%, and 10%; endometrial hyperplasia in 3%, 5%, 1%, and 2%; and cancer in 8%, 3%, 1%, and 7%. Overall, 63 patients (32%) had preinvasive or invasive lesions. Veljovich et al conclude that AGCUS on Pap smears were correlated with significant findings in 45% of patients (32% with preinvasive or invasive lesions and 13% with benign lesions). A prompt and aggressive workup was recommended.

### COMMENT BY DAVID M. GERSHENSON, MD

The classification of AGCUS was proposed as part of the Bethesda system in 1988. Not only do Veljovich et al place their findings in perspective, they also review the published reports on the subject. In seven other studies, the incidence of AGCUS was 0.48%, a figure similar to that found in the present study. In addition, the incidence of squamous intraepithelial lesions, adenocarcinoma in situ, endometrial hyperplasia, and cancer in these studies was 29.1%, 3.6%, 5.4%, and 5.8%, respectively. Recently, the American Society for Colposcopy and Cervical Pathology published guidelines for management of women with AGCUS on Pap smear. According to their recommendations, all women with AGCUS should undergo colposcopy of the cervix and vagina as well as endocervical curettage (ECC). Colposcopic-directed biopsies of abnormal areas should be performed. Patients with unqualified AGCUS who have

negative colposcopy and ECC should have a repeat Pap smear every 4-6 months until four normal smears are reported. Patients with either AGCUS favoring neoplasia or unqualified AGCUS with positive ECC should undergo cervical conization. If cells appear to be of endometrial origin, endometrial biopsy, hysteroscopy, or curettage is recommended. In summary, the message is clear: the finding of AGCUS on Pap smear should be taken very seriously since the associated incidence of both preinvasive and invasive lesions is relatively high. Appropriate workup should be performed and physicians need to counsel their patients regarding the significance of this finding. ❖

## Burning Herbs to Correct Breech Presentation

ABSTRACT & COMMENTARY

***Synopsis:*** *Moxibustion, when used in primigravidas at 33 weeks gestation, is an effective therapy for inducing an increase in cephalic presentations.*

**Source:** Cardini F, Weixin H. *JAMA* 1998;280: 1580-1584.

Moxibustion is a burning herb used to stimulate an acupuncture point beside the outer corner of the fifth toenail. To determine the efficacy and safety of moxibustion to promote version of fetuses in the breech presentation, Cardini and Weixin conducted a randomized, controlled, open clinical trial of primigravidas at 33 weeks gestation with a normal pregnancy and an ultrasound-confirmed diagnosis of breech presentation (n = 130). The moxibustion material in a "cigar-shaped roll" was applied for 30 minutes each day for seven days in the first 87 subjects, and twice daily in 43 subjects. Women in the control group (n = 130) received routine prenatal care. At 35 weeks, subjects in either group with a persistent breech presentation could elect to undergo external cephalic version (ECV). Because the beneficial effect of moxibustion may be through the stimulation of fetal activity, study subjects in both groups counted fetal movement for one hour each day.

At 35 weeks, 75.4% (98/130) of fetuses in the intervention group were in a cephalic presentation compared to 47.7% (62/130) of fetuses in the control group—a significant difference ($P < 0.001$). One patient in the intervention group had a failed ECV, while 19 of 24 ECVs in the control group were successful. Overall, even after ECV, the number of fetuses in a cephalic presentation remained significantly greater in the moxibustion-treated patients. Of note, fetal movements were significantly greater during the seven days of monitoring in the moxibustion patients, 48.45 per hour vs. 35.35 in the controls. Moxibustion treatment was not associated with adverse effects in the mother or neonate.

Cardini and Weixin conclude that moxibustion, when used in primigravidas at 33 weeks gestation, is an effective therapy for inducing an increase in cephalic presentations.

### COMMENT BY STEVEN G. GABBE, MD

There has been a significant increase in the use of alternative therapies in the United States. A nationally conducted random household telephone survey revealed that more than 40% of adults questioned used at least one of 16 alternative therapies during the past year.

The study by Cardini and Weixin, performed at two hospitals in the People's Republic of China, demonstrates that the herb moxibustion applied to a specific acupoint is associated with an increased likelihood of version in primigravid women treated during the 33rd week of pregnancy. Because there was an associated increase in fetal movement during the first week of treatment, this effect was thought to be the mechanism for the change in fetal position. Of note, the cesarean delivery rate was no different for either of the study groups—approximately 35% with most for cephalopelvic disproportion. While the trial was randomized and controlled, it was not blinded. Nevertheless, this report provides an interesting and alternative approach to the treatment of a common obstetrical problem. ❖

## *Brief Alert*

## Different Diet, Less Gas?

**Source:** King TS, et al. *Lancet* 1998;352:1187.

King and associates examined whether colonic malfermentation could be a factor in the pathogenesis of Irritable Bowel Syndrome (IBS). Six female IBS patients and six female controls were enrolled in a randomized, cross-over study in which subjects received either a standard diet (containing the usual Western foods) or an elimination diet for two weeks, followed by the alternate diet for two weeks after a two-week washout period. The elimination diet included fish and meat, but not beef, soy products replaced dairy products, and cereals other than rice were prohibited. There were also restrictions on yeast, citrus, caffeine, and tap water.

Toward the end of each two-week diet, fecal excretion

of fat, nitrogen, starch, and nonstarch polysaccharide was measured, along with a 24-hour indirect calorimetry.

On the standard diet, colonic gas production of hydrogen was two times higher in IBS patients than controls, and excretion of hydrogen plus methane was nearly four times higher. While both IBS and control subjects had reduced gas production, especially of hydrogen, while receiving the elimination diet, the IBS patients had near-normalization of their gas excretion patterns. This was associated with significant improvement in their gastrointestinal symptoms. King et al speculated that the elimination diet favorably alters the activity of certain bacteria, thereby decreasing symptoms of IBS. (*This brief alert was written by Carol Kemper, MD, Clinical Assistant Professor of Medicine, Stanford University.*) ❖

## *Pharmacology Update*

# Estradiol/Norethindrone Acetate Transdermal Systems (CombiPatch)

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

The fda has approved the first combination estrogen and progestin transdermal system for hormone replacement therapy. CombiPatch is an estrogen/progestin transdermal patch that uses a matrix patch technology that was developed by Noven Pharmaceuticals and marketed by Rhone-Poulenc Rorer. This system delivers 50 mcg of 17-estradiol and 140 mcg or 250 mcg of norethindrone acetate per day through the intact skin.[1] CombiPatch provides an alternative to oral estrogen and progestin or transdermal estrogen and oral progestin.

### Indications

CombiPatch is indicated for the treatment of moderate-to-severe vasomotor symptoms associated with menopause, treatment of vulvar and vaginal atrophy, and treatment of hypoestrogenism due to hypogonadism, castration, or primary ovary failure.

### Dosage

CombiPatch is available as a transdermal system that delivers 50 mcg of 17-estradiol or 140 mcg (9 $cm^2$) or 250 mcg (16 $cm^2$) of norethindrone acetate. For continuous combined therapy: CombiPatch 50 mcg/140 mcg should be worn continuously for 28 days. A new system should be applied twice a week during the 28-day cycle.

For continuous sequential therapy: CombiPatch 50 mcg/140 mcg should be worn for the last 14 days of the 28-day cycle following a 14-day estrogen regimen. Should a greater progestin dose be desired, CombiPatch 50 mcg/250 mcg is available.

The system should be applied on a smooth (fold-free), clean, dry area of the skin on the lower abdomen. The sites must be rotated with an interval of at least one week between sites. The patch should not be applied to or near the breast, oily areas, or areas where clothing may rub the system or modify its delivery (e.g., waistline).[1]

### Potential Advantages

CombiPatch provides an alternative to oral estrogen/progestin therapy. This transdermal system provides consistent delivery of 17-estradiol, estrone, and norethindrone over the application interval. Mean serum concentrations at steady state with application of the 50 mcg/140 mcg patches are 45 pg/mL (27-71) for estrogen, 54 pg/mL (49-72) for estrone, and 489 pg/mL (386-617) for norethindrone. Twice-weekly administration may improve medication adherence. CombiPatch has been reported to reduce triglyceride levels by 4.6% to 14.1% from baseline when measured after one year.[1] Oral hormone replacement therapy tends to increase triglyceride levels.[2]

### Potential Disadvantages

Transdermal estradiol bypasses the first past metabolism seen with orally administered estrogens and appears to have less favorable effects on the liproprotein profiles. Reductions in total cholesterol and LDL-cholesterol are less than that reported for oral estrogens.[1-3] CombiPatch also reduced HDL-cholesterol, although most of the decrease was attributed to the HDL3 subfraction—not the HDL2 subfraction.[1] Oral hormone replacement tends to increase HDL-cholesterol levels.[2] Application site reactions have been reported at a rate of up to 21%.[1]

### Comments

CombiPatch is the first transdermal product to combine estrogen and a progestin in a single patch for hormone replacement therapy. It is the transdermal counterpart to Prempro tablets (conjugated estrogen and medroxyprogesterone acetate) marketed by American Home Products and the recently approved Activelle tablets (estrogen/norethindrone acetate) marketed by Novo Nordisk. Clinical study results indicated that the product reduced the number and

daily intensity of hot flushes compared to placebo.[1] Trial results also indicated that norethindrone acetate as formulated in CombiPatch was effective in reducing the incidence of estrogen-induced endometrial hyperplasia.[1] Transdermal estrogen appears to be effective in preventing osteoporosis; however, its potential favorable effect on cardiovascular disease risk is less certain. CombiPatch is about $0.90 per day compared to $0.65 per day for oral therapy with Prempro.

### Clinical Implications

Oral hormone regimens are generally considered as first-line therapy for most postmenopausal women. Transdermal formulations may be considered for women in whom oral estrogen therapy does not relieve symptoms, is not tolerated, or women who have hypertriglyceridemia. The benefits of hormone replacement therapy include symptomatic relief, prevention of osteoporosis, and reduction of cardiovascular events. The latter has been an important reason for postmenopausal women to initiate hormone replacement therapy. Recently, the role of hormone replacement therapy in secondary prevention of CAD events and death has been questioned.[4] However, most women use hormone replacement in the role of primary prevention and data from observational studies tend to support this use. Randomized trials are under way to study the effect of estrogen replacement therapy and hormone replacement therapy both in secondary prevention and primary prevention. Results are expected in 2000-2005.[5]

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## CME Questions

**10. Soft tissue cultures in cases of presumed bacterial cellulitis:**
a. should be considered in immunocompromised patients.
b. if indicated should use local aspiration after injection of sterile saline.
c. are positive in more than 50% of cases, regardless of the method used.
d. should be accompanied by blood cultures in most instances.

**11. New bundle branch block on ECG suggests:**
a. ischemic heart disease.
b. cardiomyopathy.
c. valvular heart disease.
d. hypertrophic cardiomyopathy.

**12. The incidence of finding atypical glandular cells of undetermined significance in a Papanicolaou smear is:**
a. 0.3-0.8%
b. 0.5-1.0%
c. 1.0-1.5%
d. 2.0-5.0%
e. None of the above

**13. An increase in which of the following is thought to be the mechanism by which moxibustion contributes to a change in fetal position from breech to cephalic?**
a. Maternal temperature
b. Fetal activity
c. Uterine activity
d. Uteroplacental blood flow

**14. Combipatch (estrogen/progestin transdermal patch) is associated with:**
a. frequent episodes of breakthrough bleeding.
b. increased HDL levels.
c. reduced TG levels.
d. minimal impact on vasomotor symptoms.
e. None of the above

*By Louis Kuritzky, MD*

## Generalist and Pulmonologist Care for Patients Hospitalized with Severe COPD

Copd is the fourth leading cause of death in the United States. Comparison of generalist with specialist care of COPD has focused on ambulatory settings, but much of the cost of COPD and mortality is located in hospital settings. The current study is the first to specifically compare the care of these two professional groups in reference to inpatient COPD management.

Five academic medical centers enrolled 866 adults with severe COPD. The Therapeutic Intervention Scoring System score was used to assess intervention use on days 1, 3, 7, 14, and 25 of patient care; this system scores minor interventions like an IV or pulse oximetry 1 point, and 2-4 points for greater intensity interventions, such as arterial lines, intubation, or surgical procedures. Additionally, expenses were recorded from hospital billing records.

Both adjusted average resource intensity scores and estimated hospital costs were the same for patients treated by pulmonologists as those treated by generalists. Regueiro and associates conclude there is not a significant difference in resource use, cost, or survival of COPD patients between pulmonologists and generalists. ❖

*Regueiro CR, et al. Am J Med 1998; 105:366-372.*

## Microalbuminuria Screening in Patients with Hypertension

Increased urinary excretion of protein is a marker for future development of cardiovascular disease among hypertensive patients and correlates with the risk of mortality in diabetics. Traditional office testing materials for albumin requires at least 300-500 mg/d albumin excretion to indicate a positive test; since much lower levels of urinary albumin excretion (UAE) are abnormal (normal is < 30 mg/d), there has been a window wherein abnormal UAE may be missed in typical outpatient practice, unless the clinician resorts to the somewhat cumbersome and expensive 24-hour urine analysis.

In diabetics, interventions addressed at improving microalbuminuria with ACE inhibitors have shown less progression to overt nephropathy. Hence, it has been felt that early detection of even modest levels of UAE above normal is desirable. For this purpose, the Micral-Test (Boehringer Manheim, Indianapolis, IN) has been developed. The current study is the first to evaluate its efficacy in hypertensive patients.

In a patient population of 171 hypertensives, Micral-Test was compared with 24-hour urine collection. The sensitivity of random urine sampling was 92%. Equally valuable as the high sensitivity, Gerber and colleagues acknowledge a small (≤ 5%) false-positive rate. Gerber et al conclude that Micral-Test is a valuable screening tool for microalbuminuria. ❖

*Gerber LM, et al. Am J Hypertens 1998;11:1321-1327.*

## Mortality Results for Early Elective Surgery or Ultrasonographic Surveillance for Small Abdominal Aortic Aneurysms

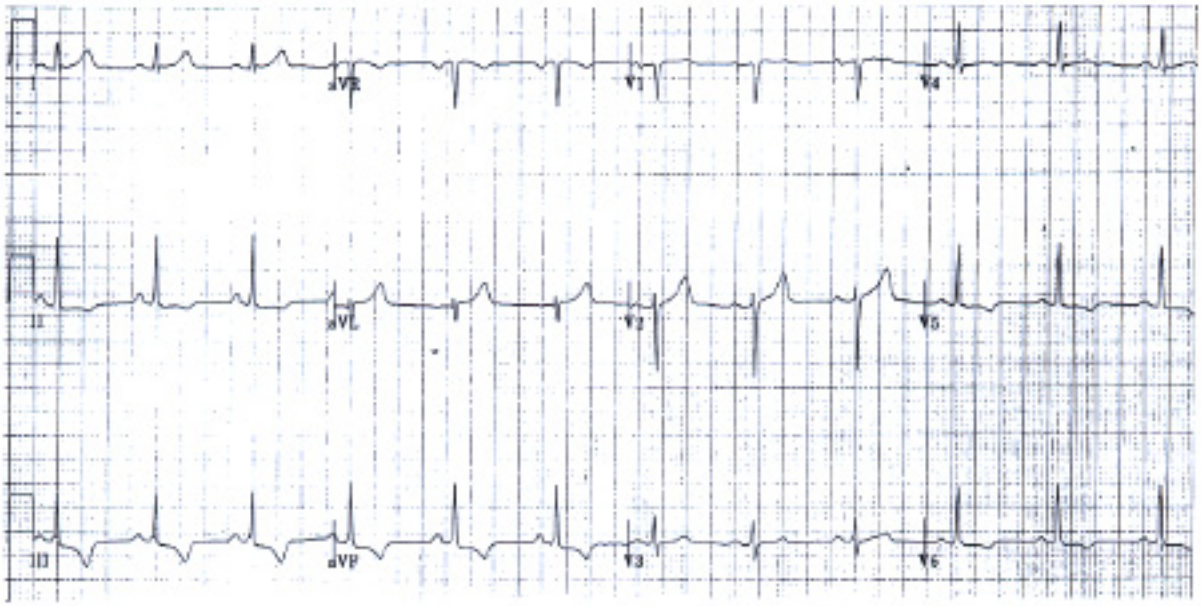
Although elective repair of large abdominal aortic aneurysms (AAA) reduces mortality, small aneurysms are often followed by observation with repeat ultrasonographic measurement. Unheralded rupture of an AAA is always associated with a high mortality rate, hence, the potential for elective early intervention is theoretically attractive. This study compared, in patients older than 60 years (n = 1090), elective surgical repair of small AAA (4.0-5.5 cm) vs. ultrasonographic surveillance for 4-6 years. Ultrasound was performed every six months for AAA 4.0-4.9 cm, and every three months for AAA 5.0-5.5. Additionally, if growth rate was greater than 1 cm/yr or if AAA became tender or symptomatic, surgery was offered to the patient. Statistical analysis of overall mortality by intention-to-treat methodology was performed.

In the first 30 days of the trial, the 5.8% mortality rate seen in the surgical group provided a statistical disadvantage. At all end point times, the surgical group enjoyed no advantage over ultrasonographic surveillance. The authors conclude that early surgical intervention is not advantageous over ultrasonographic surveillance in terms of mortality for AAA less than 5.5 cm. ❖

*The UK Small Aneurysm Trial Participants. Lancet 1998;352:1649-1655.*

# T Wave Inversion after PSVT Conversion

*By Ken Grauer, MD*




12-lead ECG obtained from a 42-year-old man shortly after conversion of PSVT to normal sinus rhythm. All symptoms have resolved at the time this tracing is recorded.

**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 has now 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:

**Pharmacology Update: Celebrex**

**Intracavernous Vasoactive Drugs in Persistent Psychogenic Erectile Dysfunction Treatment**