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ABSTRACT & COMMENTARY

Association of Seafood Consumption and Brain Mercury Levels with Brain Neuropathology

By Harold L. Karpman, MD, FACC, FACP

Clinical Professor of Medicine, UCLA School of Medicine

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

SYNOPSIS: Although moderate seafood consumption was correlated with higher brain levels of mercury, these levels were not correlated with brain neuropathology.

SOURCE: Morris CM, Brockman J, Schneider JA, et al. Association of seafood consumption, brain mercury level, and APOE e4 status with brain neuropathology in older adults. *JAMA* 2016;315:489-497.

Numerous studies have found protective associations between seafood consumption and dementia.[1-5] However, seafood is also a source of mercury, a neurotoxin that may impair neurocognitive development.[6] Previous research shows selenium reduces mercury toxicity.[7] Morris et al studied whether seafood consumption is correlated with increased brain mercury levels, the relationship of these mercury levels to selenium, and also whether seafood consumption or brain mercury levels are correlated with brain neural pathologies.[8]

Morris et al carefully analyzed autopsied cases of deceased participants in the Rush Memory and Aging Project (MAP) who died between November 2004 and November 2015 and who had completed a dietary assessment before death. The MAP study is an ongoing clinical, neuropathological cohort study of older adults that began in 1997 and included residents of retirement communities and subsidized housing in Chicago.[9] The blood mercury levels of 286 autopsied brains of 544 deceased participants were positively correlated with the number of seafood meals they consumed per week. Seafood consumption was significantly correlated with less Alzheimer's disease pathology, including lower

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density of neuritic plaques, less severe and widespread neurofibrillary tangles, and a lower frequency of neuropathologically defined Alzheimer's disease — but only among apolipoprotein E (APOE e4) carriers.[8] Fish oil supplementation had no statistically significant correlation with any neuropathologic marker. The authors concluded that higher brain concentrations of mercury were not significantly correlated with increased levels of brain neuropathology.

■ COMMENTARY

Morris et al derived their findings from a dated, largely non-Hispanic Caucasian cohort. As a result, these findings may not be generalizable to younger adults or other racial or ethnic groups.[8] Other study limitations were the subjective measure of dietary intake and the observational study design. However, the results of this study suggest that although seafood consumption was correlated with higher brain levels of mercury, these levels were not correlated with brain neuropathology, and that from a clinical point of view, moderate seafood consumption was correlated with a lesser burden of brain Alzheimer's disease neuropathology. This latter finding is reassuring. Ingested mercury accumulates in the body over decades. The absence of an increased risk of Alzheimer's disease or dementia related to mercury in this study suggests patients can consume seafood without substantial concern of mercury contamination diminishing its possible cognitive benefit in older adults. Since eating fatty fish has been considered potentially beneficial against cognitive decline in at least a proportion of older adults, it appears from the study results that patients who consume fish generally should not be concerned about the effects of possible mercury contamination from eating fish. ■

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ABSTRACT & COMMENTARY

Trimethoprim-sulfamethoxazole vs. Placebo for Skin Abscesses After Incision and Drainage

By Richard R. Watkins, MD, MS, FACP

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Dr. Watkins reports that he receives research support from Actavis.

SYNOPSIS: A multicenter, double-blind, randomized, clinical trial found that a seven-day course of trimethoprim-sulfamethoxazole following incision and drainage (I&D) resulted in a higher rate of cure for skin abscesses compared to I&D and placebo.

SOURCE: Talan DA, Mower WR, Krishnadasan A, et al. Trimethoprim-sulfamethoxazole versus placebo for uncomplicated skin abscess. *N Engl J Med* 2016;374:823-832.

A skin abscess is a common presenting complaint in EDs, especially since the emergence of community-associated methicillin-resistant *Staphylococcus aureus* (MRSA). Incision and drainage (I&D) is the primary treatment, and antibiotics have been considered adjunctive. Talan et al aimed to clarify the role for trimethoprim-sulfamethoxazole (TMP-SMX) in treating skin abscesses after I&D and determine if this drug leads to a higher rate of cure.

This double-blind, randomized, clinical trial compared a seven-day outpatient course of TMP-SMX (320 mg/1,600 mg) twice a day to placebo in patients with cutaneous abscesses who received I&D in the ED. Patients older than 12 years of age were enrolled from five EDs between April 2009 and April 2013. They all presented with a skin abscess that existed for less than a week and measured at least 2 cm in diameter. The primary outcome was clinical cure of the abscess, which was determined seven to 14 days after the end of the treatment period.

Researchers randomized 630 patients to receive TMP-SMX, while 617 received placebo. Their median age was 35 years (range, 14-73 years) and 58.2% were male. MRSA grew in 45.3% of the wound cultures, and 97.4% of the strains were susceptible to TMP-SMX. The abscess cure rate was 80.5% in the TMP-SMX group compared to 73.6% in the placebo group ($P = 0.005$) in the modified intention-to-treat population, which included all participants who took at least one dose of TMP-SMX or placebo. In the per-protocol group, which included patients who took ≥ 75% of the total doses of study drug during the first five days and experienced a test-of-cure visit, clinical cure for those who received TMP-SMX was 92.9% vs. 85.7% for placebo ($P < 0.001$). TMP-SMX was superior to placebo for most of the secondary outcomes, including lower rates of subsequent surgical drainage procedures, skin infections at a new site, and infections among household members. Gastrointestinal symptoms were the most common adverse events, which occurred among 42.7% in the TMP-SMX group and 36.1% in the placebo group.

■ COMMENTARY

The decision to prescribe oral antibiotics for uncomplicated skin abscesses after I&D has been controversial. The potential benefits, including faster healing, reduced future occurrences, and decreased transmission to household contacts, must be weighed against the risks of side effects, potentially spreading antibiotic resistance, *Clostridium difficile* infection, and the cost of medication. The 2014 Infectious Diseases Society of America guidelines recommend antibiotics after I&D for patients with impaired host defenses or evidence of systemic inflammatory response syndrome, including temperature > 38°C or < 36°C, tachypnea > 24 breaths per minute, tachycardia > 90 beats per minute, or white blood cell count > 12,000 or < 4,000 cells/µL, which is based on moderate-quality evidence.[1] Of the five studies cited for this recommendation, only two were conducted during the current MRSA era: one included children and one included adults. The latter was a multicenter, double-blind, randomized, placebo-controlled trial that found treatment with TMP-SMX after I&D did not reduce treatment failure but did decrease the formation of subsequent lesions.[2] However, this study and others have been criticized for being underpowered because the cure rate with I&D alone exceeds 80% and large sample sizes are necessary to test for small differences in cure rates.

The Talan et al study provides some welcome clarity to the role for antibiotics after I&D. Their study was large, well-designed, and found a significant benefit for a seven-day course of TMP-SMX. The low rate of adverse events with TMP-SMX was surprising, since this drug is one of the most frequent antibiotics to cause adverse reactions, including ones that lead to ED visits.[3] Although the risks associated with antibiotics are well known, one also must appreciate that higher cures of primary abscesses will subsequently lead to reduced costs from fewer follow-up visits, surgeries, hospitalizations, and less spreading of infection to others in households and communities. Although it is the latest, the Talan et al study will likely not be the last on the topic. Clinicians must manage cutaneous abscesses based on careful interpretation of the available data. Therefore, after a frank discussion with the patient about the risks and benefits, a seven-day course of an antibiotic with MRSA activity (e.g., TMP-SMX or doxycycline) should be prescribed after I&D of a moderate-sized (≥ 2 cm) cutaneous abscess. ■

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ABSTRACT & COMMENTARY

Early Chest CT Can Improve Treatment for Community-acquired Pneumonia

By Samuel Nadler, MD, PhD

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

SYNOPSIS: In patients with suspected community-acquired pneumonia, early chest CT significantly changed management decisions.

SOURCE: Claessens YE, Debray MP, Tubach F, et al. Early chest computed tomography scan to assist diagnosis and guide treatment decision for suspected community-acquired pneumonia. *Am J Respir Crit Care Med* 2015;192:974-982.

Community-acquired pneumonia (CAP) is a very common diagnostic consideration. Early diagnosis and administration of antibiotics can save lives. However, the clinical diagnosis is often uncertain and misdiagnosis is frequent. This leads to inappropriate treatment with unnecessary antibiotics and may obscure the real underlying diagnosis. Even chest radiographs (CXRs) demonstrating abnormalities can be misleading, and the concordance of interpretations of these infiltrates is poor, regardless of practitioner experience.[1] Thus, reliance on clinical factors and CXRs may lead to misdiagnosis and mistreatment of many patients presenting with respiratory disease.

This study hypothesized that the use of early CT of the chest would improve the diagnosis and subsequent management of CAP. This was a prospective, interventional study in four tertiary teaching hospitals between November 2011 and January 2013. Enrolled in this study were 319 adults older than 18 years of age who presented to the ED with suspicion of CAP. The criteria for CAP included: new onset of systemic symptoms (sweats, chills, aches, temperature > 38°C or < 36°C) and symptoms of lower respiratory tract infection (cough, sputum, dyspnea, chest pain, or altered breath sounds). Exclusions included: pregnancy, hospice patients, inability to complete the study, CURB-65 score of 3 or higher, or the need for ICU admission. A local radiologist performed CXRs and reported findings in a standardized fashion. Multi-detector chest CT using a low-dose protocol was performed as soon as possible afterward and was similarly interpreted. At this point, the ED physician completed a clinical report assigning a pneumonia probability and treatment plan. Three independent evaluators who were experts in pulmonary medicine, infectious disease, or radiology subsequently adjudicated each assessment and defined the likelihood of CAP based on clinical and radiographic data and assigned a probability of CAP (definite, probable, possible, or excluded). Each case was then re-evaluated using data from the time of clinical discharge up to day 28 and assigned a final probability category.

After the initial clinical assessment and chest radiograph, the percentages of patients assigned to the CAP probability categories of definite, probable, possible, or excluded were 44.9%, 36.9%, 16.9%, and 1.2%, respectively. After chest CT, these categories shifted to 50.9%, 10.9%, 9.4%, and 28.8%, respectively. Adjudicating committee assignments were 47%, 8.7%, 11.3%, and 32.9%, respectively. At the 28-day final adjudication, the distribution was 47%, 4.1%, 10.7%, and 38.2%, respectively. Interestingly, of the 120 patients without parenchymal infiltrates on CXR, 40 had infiltrates on CT that conventional CXR missed. Conversely, of the 188 patients with parenchymal infiltrates on CXR, CT scans excluded CAP in 56 patients. Based on these CT findings, the ED physician modified the probability of CAP diagnosis in 187 of the patients (58.6%; 95% confidence interval, 53.2-64.0%). Of these patients, 59 were upgraded and 128 downgraded based on CT, including 11 of 36 patients previously considered as definite CAP by CXR.

■ COMMENTARY

This was an intriguing study that clearly showed the limitations of clinical factors and CXRs to diagnose CAP. More than half (58.6%) of the pre-CT probabilities of CAP were altered after chest CT. Prior to chest CT, 64.7% of patients were intended to start antibiotic therapy and after chest CT, researchers ended the administration of antibiotics in 29 patients. Furthermore, 51 patients who did not receive antibiotics after CXRs were then administered therapy after receiving a CT scan. Three pulmonary emboli were discovered, and cardiac failure was diagnosed in 11 patients. Furthermore, 45 patients had a change in level of care, including 22 outpatients being admitted and 23 admissions changed to discharges. Overall, modifications of antibiotics or site of care occurred in 60.8% of patients.

It appears that most of the changes in diagnostic probability were in marginal cases. The percentage of "probable" CAP cases decreased with progressive assessments from 36.9% with CXR and clinical suspicion alone, to 10.9% after CT, to 8.7% after committee adjudication, and to 4.1% at 28 days. The number of "possible" cases decreased from 16.9% to 9.4% with chest CT. In a univariate secondary analysis, among 188 out of 308 patients with an infiltrate on CXR, CT excluded CAP in 56 patients. These patients, compared to the 132 with infiltrates confirmed on CT, tended to be older (71.1 vs. 63.2 years of age; $P = 0.0131$), have lower white blood cell (WBC) counts (10.2 vs. 12.6 x $10^3/mm^3$; $P = 0.283$) and lower C-reactive protein (CRP) levels (78 vs 163.3 mg/L; $P = 0.0074$). Conversely, among 120 patients without infiltrates on CXR who also had a CT, 40 patients had CT infiltrates compatible with CAP. Compared to the 80 patients without CT infiltrates, those 40 patients with CT infiltrates were more likely to have crackles on exam (48.7% vs. 26.6%; $P = 0.0169$), higher WBC counts (12.3 vs. 10.2 x $10^3/mm^3$; $P = 0.0387$), and higher CRP levels (138.1 vs. 59.9 mg/L; $P = 0.0037$). Thus, clinical factors such as lung auscultation and CRP still seem to have a good predictive value for CAP.

Ultimately, the decision to use CT scanning for the diagnosis of CAP will require a thorough analysis of the cost of care and the outcomes data. It may very well be that the improved diagnostic accuracy of CT scanning will reduce the cost of care enough to offset the cost of additional CT scans. Furthermore, earlier administration of antibiotics with CT-confirmed CAP and prevention of unnecessary antibiotics in those without CAP might also improve health outcomes. Both these factors should be prospectively examined before entertaining the widespread adoption of routine CT for the diagnosis of CAP. ■

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PHARMACOLOGY UPDATE

Infliximab-dyyb for Injection (Inflectra)

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

Dr. Elliott is Medical Director, Pharmacy, Northern California Kaiser Permanente, and Assistant Clinical Professor of Medicine, University of California, San Francisco. Dr. Chan is Pharmacy Quality and Outcomes Manager, Kaiser Permanente, Oakland, CA.

Drs. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has approved infliximab-dyyb, a biosimilar to the reference drug infliximab (Remicade). The approval represents the first biosimilar monoclonal antibody approved in the United States. Infliximab is a chimeric, monoclonal antibody directed to anti-tumor necrosis factor (TNF). Infliximab-dyyb is marketed as Inflectra. The FDA announced that biological products licensed under the Public Health Services Act must bear a nonproprietary name that includes an FDA-designated four-digit suffix in lowercase letters (in this case "dyyb") to distinguish products that have not been determined to be interchangeable and help with pharmacovigilance.[1] The biosimilar is approved in Europe where it is marketed as Remsima.

INDICATIONS

Infliximab-dyyb is indicated for the treatment of Crohn's disease (adults and pediatric), ulcerative colitis, rheumatoid arthritis (RA) with methotrexate, ankylosing spondylitis (AS), psoriatic arthritis, and plaque psoriasis.[2]

DOSAGE

The dosage is the same for infliximab (Remicade). Infliximab-dyyb is available as 100 mg lyophilized powder for IV infusion.

POTENTIAL ADVANTAGES

Infliximab-dyyb offers another, possibly less expensive, option for treatment of a number of autoimmune conditions.

POTENTIAL DISADVANTAGES

Infliximab-dyyb is currently not approved as interchangeable to infliximab.

COMMENTS

Biosimilars are biological products that are highly similar to the reference product notwithstanding minor differences in clinically inactive components. There are no clinically meaningful differences between the biological product and the reference product in terms of the safety, purity, and potency of the product.[3] The FDA has determined that infliximab-dyyb

meets the criteria of biosimilarity based on structural and functional characteristics, animal and human data, clinical effectiveness, safety, and immunogenicity.[4] Two clinical trials have been published.[5,6] Both were 54-week, randomized, parallel-group studies comparing infliximab-dyyb to infliximab in terms of efficacy, safety, pharmacokinetics, and immunogenicity. One was in patients presenting with RA not adequately controlled on methotrexate (n = 606) and the other in patients presenting with AS (n = 250). In RA, the primary efficacy endpoint was a 20% improvement in the American College of Rheumatology criteria (ACR20). Response rates were similar (74.7% for infliximab-dyyb vs. 71.3% for infliximab). Other efficacy endpoints (disease activity scores) were similar, as well as immunogenicity (antidrug antibodies) and frequencies of treatment-related adverse events. For AS, the efficacy endpoint was 20 and 40% improvement in Ankylosing Spondylitis Disease Activity Score (ASAS20/ASAS40). Response rates, safety, pharmacokinetics, and immunogenicity were similar between the biosimilar and infliximab. There is a study underway assessing the safety and efficacy of switching from infliximab to infliximab-dyyb in RA, spondyloarthritis, psoriatic arthritis, ulcerative colitis, Crohn's disease, and chronic plaque psoriasis.[7] Final data collection is expected to be completed in July 2016.

CLINICAL IMPLICATIONS

Infliximab-dyyb is the first approved biosimilar monoclonal antibody. It is approved for all the indications as infliximab (Remicade), with the exception of pediatric ulcerative colitis. It is currently not designated as interchangeable, which means it cannot be substituted for the reference product without provider approval. Cost was not available at the time of this review. Hospira/Pfizer may still face patent challenges from Johnson & Johnson regarding a patent that expires in September 2018, even though the U.S. Patent and Trademark Office has previously rejected the challenge by Johnson & Johnson.[8] ■

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CME QUESTIONS

1. **Moderate seafood consumption:**
   a. is correlated with increased Alzheimer's disease neuropathology.
   b. is correlated with decreased Alzheimer's disease neuropathology.
   c. is correlated with brain neuropathology.
   d. None of the above

2. **According to the study by Claessens et al., which of the following statements is true?**
   a. Clinical factors without chest radiographs accurately diagnosed community-acquired pneumonia (CAP) in almost every case.
   b. Chest CT rarely altered management decisions in patients with suspected CAP.
   c. In patients with high CURB-65 scores, chest CT was unnecessary.
   d. Chest CT significantly increased the number of patients in whom CAP was excluded as a diagnostic consideration.

Clinical Briefs

By Louis Kuritzky, MD

Home BP Monitoring vs. Ambulatory BP Monitoring

SOURCE: Shimbo D, Abdalla M, Falzon L, et al. *J Am Soc Hypertens* 2016;10:224-234.

For the last several decades, decisions about management of hypertension (HTN) have been based predominantly on blood pressure (BP) recorded in an office, commonly known as "office BP" (OBP). Randomized, interventional HTN trials based on OBP have confirmed important clinical benefits from treatment: reductions in myocardial infarction of about 25%, stroke of about 40%, and heart failure > 50%. Nonetheless, vocal supporters for 24-hour ambulatory blood pressure monitoring (ABPM) have pointed out that ABPM correlates significantly better with cardiovascular disease (CVD) outcomes than OBP, leading to the logical conclusion that treatments based on ABPM might also provide better CVD risk reduction.

The same arguments can be made for home BP monitoring (HBPM). Since both ABPM and HBPM provide the opportunity for many more BP readings than occasional OBP, it's not surprising that either tool has better positive predictive value than OBP. Additionally, HBPM and ABPM definitions of HTN appear to be more accurate because they eliminate most white-coat HTN.

Shimbo et al performed a systematic review of ABPM and HBPM trials. While the authors were able to confirm that both ABPM and HBPM have stronger association with CVD than OBP, they were unable to determine whether one holds a distinct advantage over the other. Although clinical trials with ABPM seem to indicate a stronger association with CVD than observed in HBPM trials, trial data that include both methods of BP monitoring (ABPM and HBPM) in the same study population are few. Concordant with recent (2015) U.S. Preventive Services Task Force recommendations, clinicians should routinely use ABPM or HBPM prior to initiating treatment for HTN. ■

Who's Right About DPP4 Agents and Heart Failure?

SOURCE: Filion KB, Azoulay L, Platt RW, et al. *N Engl J Med* 2016;374:1145-1154.

Opinions about DPP4 inhibitors (e.g., sitagliptin, saxagliptin) and heart failure (HF) have vacillated between "worry" and "don't worry" for about two years. In the March 24, 2016, edition of the *New England Journal of Medicine*, results of an analysis performed by the Canadian Network for Observational Drug Effect Studies indicate that there is no demonstrable increase in risk for HF, as indicated by hospitalization for HF, with incretin agents (GLP1 analogues and DPP-4 inhibitors). Their conclusions are based on an evaluation of data from 29,741 hospitalizations for HF among 1.5 million patients in the United States, Canada, and the United Kingdom.

On April 6, the FDA issued a "new alert" about the potential for increased risk of HF with saxagliptin (Onglyza) and alogliptin (Nesina), as well as any combination products that contain either of these two agents.

Who's right? The FDA warnings should be taken seriously, even if other evaluators disagree — if only to maintain an appropriate standard of care. Hence, avoid prescribing the DPP4 inhibitors saxagliptin or alogliptin to patients with HF until the FDA provides further advice. In the meantime, the association with HF has not been deemed a "class effect." Therefore, other DPP4 inhibitors such as sitagliptin or linagliptin, which were not named by the FDA as proscribed for patients with HF, should be considered when clinicians wish to use a DPP4 inhibitor in patients with HF. ■

Severe Hypoglycemia: Identifying At-risk Groups

SOURCE: Pathak RD, Schroeder EB, Seaquist ER, et al. *Diabetes Care* 2016;39:363-370.

There are numerous reasons to show a healthy respect for hypoglycemia in diabetic patients. First, hypoglycemia is responsible for many deaths in diabetics. Second, hypoglycemia may cause consequential injuries from falls and auto accidents. Third, hypoglycemia is included in the American Diabetes Association treatment algorithm list of five issues clinicians should address routinely when advancing pharmacologic treatment from metformin to polypharmacy. Fourth, patients often weigh issues about hypoglycemia risk as highly important in their decision process about advancing and adhering to medication.

Pathak et al reported results of an observational cohort study of almost 1 million adults participating in the Surveillance, Prevention, and Management of Diabetes Mellitus (SUPREME-DM) network who were treated during the 2005-2011 interval. Severe hypoglycemia was diagnosed among inpatients and patients presenting to EDs. Statistically significantly higher rates of severe hypoglycemia occurred in older patients (especially those > 75 years of age) and those with chronic kidney disease, heart failure, cardiovascular disease, and depression. Pharmacologic agents associated with higher risk of severe hypoglycemia included insulin, insulin secretagogues, and beta-blockers.

Because hypoglycemia is such an important obstacle to optimized goal attainment in diabetes, clinicians may wish to factor the above-mentioned demographics into their pharmacologic decision process. ■

Internal Medicine [ALERT]

ECG Review

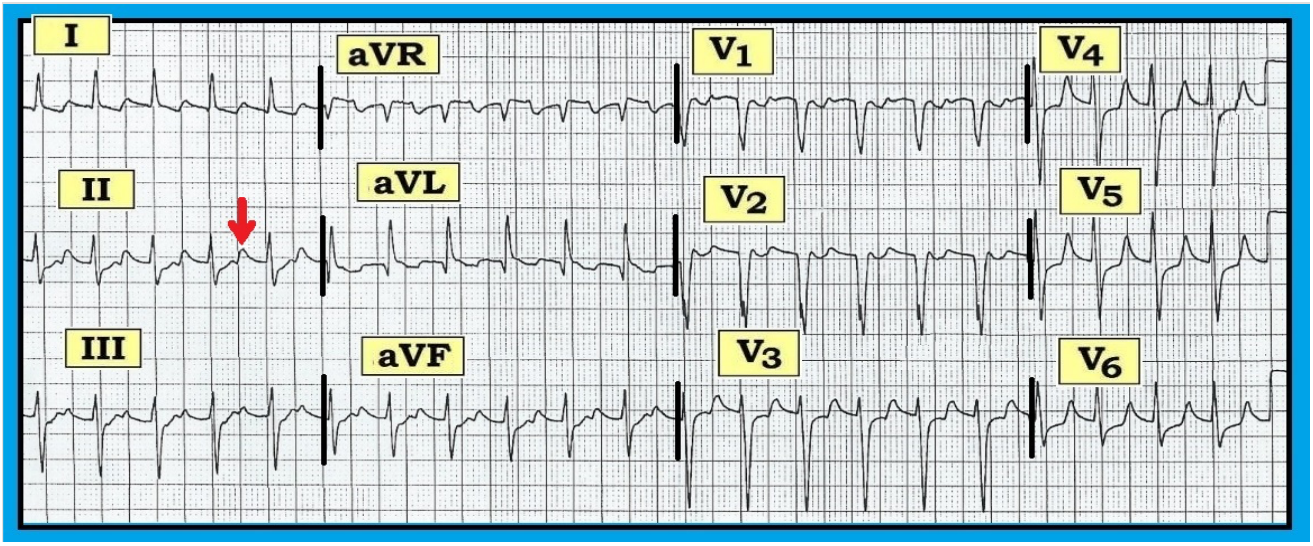
By Ken Grauer, MD

Professor Emeritus in Family Medicine, College of Medicine, University of Florida

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

SVT in a 13-Year-Old Patient

The ECG in the figure below was obtained from an otherwise healthy 13-year-old boy. He was alert and hemodynamically stable at the time this ECG was recorded. How should one interpret this tracing? Is there a clue on the tracing as to the mechanism of the arrhythmia?



The patient is hemodynamically stable. The rhythm is rapid and regular. The R-R interval is just over two large boxes in duration, which means that the ventricular rate is just under 150/min. The QRS complex is narrow (i.e., not more than half a large box in duration). Sinus P waves are absent. The red arrow in lead II points to a T wave, not a P wave. This description fits a regular supraventricular, or narrow-complex tachycardia (SVT), without sinus P waves.

The three principal diagnostic considerations for a regular SVT rhythm without sinus P waves are: 1) a reentry form of SVT, in which the reentry circuit is contained within the AV node; 2) atrial flutter; or 3) sinus tachycardia, in which sinus P waves are hidden within the preceding T wave. Atrial flutter is extremely uncommon in an otherwise healthy child. In addition, other than perhaps in lead I, there is no suggestion of a sawtooth flutter pattern on this tracing. The rhythm in the figure is also not sinus tachycardia because retrograde atrial activity is present, and therein lies the key to identifying the mechanism of this arrhythmia. AV nodal reentry forms of SVT (commonly referred to as AVNRT) are characterized by the presence of a regular, narrow-complex tachycardia at a rate between 130-240/min, without normal sinus P waves. Sometimes, retrograde P waves may be seen in some leads during tachycardia as a notch in the terminal portion of the QRS. This notch reflects conduction of the impulse back to the atria each time there is a QRS, which is why the notch appears as a negative deflection in the inferior leads. In contrast, retrograde atrial activity typically appears as a positive deflection in more superior leads, such as aVR or V1. Because the reentry circuit with AVNRT is contained within the AV node, retrograde conduction to the atria is usually quite fast. When seen, the notch most often will appear very close to the QRS complex. On the other hand, in patients with Wolff-Parkinson-White (WPW) syndrome, reentry forms of SVT typically involve retrograde conduction over an accessory pathway (AP) that is situated further away because the AP lies outside and at some distance from the AV node. The reentry circuit of such patients with WPW is therefore longer, and the RP interval (i.e., distance from the QRS complex to the retrograde P wave) is correspondingly greater.

Retrograde conduction during the tachycardia with a long RP interval clearly appears in the figure as a negative notch in the inferior leads (just before the red arrow in lead II) and as a positive notch at the very end of the T wave in leads aVR and V1. This finding should strongly suggest that this 13-year-old boy is predisposed to tachycardia episodes because of the presence of an "occult" accessory pathway. No delta wave appears on the ECG, because conduction to the atria over this AP is retrograde.

Please visit http://tinyurl.com/ACLS-14-PSVT for more on the mechanism of reentry SVT rhythms (See Section 14.3.7).