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INSIDE

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A Placebo the Patient Believes in is Effective for the Common Cold

ABSTRACT & COMMENTARY

By Joseph E. Scherger, MD, MPH

Vice President, Primary Care, Eisenhower Medical Center; Clinical Professor, Keck School of Medicine, University of Southern California

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

Synopsis: *A randomized, controlled trial of persons with new onset common cold showed modest effects of placebo on duration and severity of the cold symptoms, but greater effects among the patients who believe in the benefits of echinacea, whether receiving the supplement or placebo.*

Source: Barrett B, et al. Placebo effects and the common cold: A randomized controlled trial. *Ann Fam Med* 2011;9:312-322.

THERE IS A LONG HISTORY OF RESEARCH ON THE POWER OF THE PLACEBO. The authors of this article cite a 1955 paper by Beecher, "The Powerful Placebo," that looked at 15 studies involving more than 1000 patients. Beecher famously claimed that the "placebo effect" was 35.2% in many conditions.[1] In subsequent research, the evidence of placebo effects is strongest for pain and depression.[2,3] For the common cold, Eccles reported that a review of clinical trials on the effects of cough medications demonstrates that 85% of the reduction in cough comes from the placebo effect and only 15% from the active ingredient.[4]

This study was done by a team at the University of Wisconsin active in research in integrative medicine. The study was funded by the National Center for Complementary and Alternative Medicine at the National Institutes of Health. A total of 719 persons with new onset common cold, aged 12 to 80, were randomized into four groups: those receiving no pills; those blinded to placebo; those blinded to echinacea; and those given open-label echinacea. Then mean duration of the cold was 7.03 days in the no pill group. The three groups receiving pills

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had a reduction in cold symptoms by an average of about ½ day, and a reduction in severity of symptoms of 10-20%. Interestingly, and contrary to the hypothesis of the investigators, those receiving open-label echinacea did not have any greater benefit than those who were blinded. However, among the 120 persons who reported a belief that echinacea was effective, their illness duration was 2.58 days shorter with 26% less severity than the rest of the participants, whether they received open-label echinacea or placebo.

■ COMMENTARY

Belief in a therapy is a powerful therapeutic agent. We should be careful not to dispel our patient's beliefs, especially when these beliefs are not harmful. Beliefs in treatments for the common cold are widespread, including alleged benefits of echinacea, Airborne, and zinc. These treatments have been shown to be largely a placebo; however some people swear they work, and with this belief, they do!

This study was designed in 2002 at a time when there was widespread belief and some clinical evidence in the effectiveness of echinacea for the common cold. Then came four highly publicized negative clinical trials of echinacea and the study team noticed a change in belief among the study participants in echinacea during the four years of recruiting and randomizing patients. They suggest that this may have caused the modest effects of the open-label echinacea seen in the results.

As physicians, our job is to help our patients. When they are sick, we do what we can to help them get better. Our job is not to lecture patients on what the current clinical evidence is for any given treatment, a changing knowledge base anyway, when such information is not helpful in treating the patient. I do not recommend my patients spend their money on placebos they have no belief in. I do not promote unscientific beliefs. However, when patients express that they will go out and get echinacea for their cold since it always works for them, I say fine. This study shows that the patients are right, and that their belief is the therapeutic agent. ■

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Please call **Neill Kimball**, Managing Editor, at (404) 262-5404.

Secondary Prevention of Postherpetic Neuralgia

ABSTRACT & COMMENTARY

By Allan J. Wilke, MD

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Dr. Wilke reports no financial relationship to this field of study.

Synopsis: *Adding gabapentin to valacyclovir early in the treatment of acute herpes zoster may reduce the incidence of postherpetic neuralgia.*

Source: Lapolla W, et al. Incidence of postherpetic neuralgia after combination treatment with gabapentin and valacyclovir in patients with acute herpes zoster: Open-label study. *Arch Dermatol* 2011;147:901-907.

Postherpetic neuralgia (PHN), pain persisting longer than 3 months after development of a rash, is the most common complication of herpes zoster (HZ). It can be severe, especially in the elderly, with age being the most important factor in predicting its development. The worst cases are very difficult to treat and can sometimes last for months to years. This group of researchers from Texas re-

port on an uncontrolled, open-labeled study performed in a private dermatology clinic that tested the hypothesis that treatment of acute HZ with a combination of gabapentin and valacyclovir would prevent PHN.

Between February 2002 and October 2007, they approached consecutive adults who presented to their office with acute HZ. Their inclusion criteria included age ≥ 50 years, a clinical diagnosis of uncomplicated HZ presenting within the first 72 hours of vesicles, and an average pain score ≥ 4 on the 10-point Likert scale. Moderate pain was defined as 4-6, and severe pain as 7-10. They had a large number of exclusion criteria including: women who had even the slightest chance of becoming pregnant or were already pregnant or nursing; patients with immune dysfunction or who were receiving immunosuppressive therapy; patients treated with medications directed against the herpesvirus; patients currently receiving gabapentin or a tricyclic antidepressant; patients with liver or renal problems; and patients with ocular involvement of HZ. The investigators recruited 133 subjects, with an average age of 65. Most were white. Two-thirds were female. On presentation, 62% rated the pain ≥ 7. Patients accepted into the study received 1000 mg caplets of valacyclovir, which they took three times a day for 7 days. They were also started on gabapentin 300 mg per day, which was increased weekly to a goal of 3600 mg per day in three divided doses, based on patient tolerance and side effects. At 4 weeks, pain was reassessed. If it was < 4, then gabapentin was stopped. Otherwise, it was continued for another 4 weeks. In either case, discontinuing it was accomplished by tapering it over 1 week. Patients were allowed to continue other pain medication. The subjects had frequent follow-up, at which time pain, sleep disturbance, use of analgesics, and any abnormal sensations were recorded. In addition, quality-of-life questionnaires were collected at each visit.

The endpoint of interest was the presence of pain at 3, 4, and 6 months. Thirty-seven (37) subjects were lost to follow-up; almost half of them reported no pain at their last visit. At 6 months, 9.8% of subjects still reported some pain; 6.8% rated pain > 3. Patients who presented with severe pain were more likely than patients with moderate pain to have pain at the study's end, although this did not achieve statistical significance. There was a trend for patients older than 70 to have persistent pain compared to younger subjects, but again, this was not statistically significant. There was no gender difference. Quality-of-life scores improved for all participants during the course of the study.

■ COMMENTARY

The main weakness of this study is its design. It was neither blinded nor randomized. Secondly, the site of this study was a private dermatology clinic; these patients may differ from those who present to a primary care office.

The reported prevalence of PHN varies wildly, depending on where the study was conducted. For instance, a study in an Icelandic general practice reported a prevalence < 7% in patients older than 60 at 3 months.[1] A meta-analysis of studies that evaluated the efficacy of acyclovir in treating acute HZ estimated a prevalence of 21%.[2] A population-based study from the Mayo Clinic reported 33% in subjects ≥ 79 years of age.[3] The discrepancy probably relates to the methods of patient recruitment to drug trials, the referral of more severely afflicted patients to specialty clinics (as may have occurred in the current study), the rigor of recording data, and how patients are questioned about pain (quantitative vs qualitative assessment).

The prevention of PHN recalls the phrase, "The best defense is a good offense." Preventing HZ is possible through vaccination.[4] Varicella-zoster vaccine (Zostavax) for the prevention of shingles reduces the incidence of HZ by 51%. Subjects who received the vaccine and went on to develop HZ had a 39% reduction in PHN.[5] Unfortunately, the vaccine has not been widely used for reasons that are both economic and operational; only 2-7% of eligible people have been vaccinated.[6] Merck sells the vaccine to the federal government for about $160, making it the most expensive adult vaccine,[7] but the good news is that Medicare Part D covers it. It needs to be stored in a freezer. In March of this year, the Food and Drug Administration (FDA) lowered the age for the use of zostavax to 50 years. The vaccine is not 100% effective, and there will always be people who go unvaccinated, so having an effective treatment to prevent PHN would be welcomed.

Currently, valacyclovir and famciclovir are recommended for the treatment of HZ. Twenty years ago, before we had those medications, Whitley and colleagues used acyclovir with prednisone to treat HZ.[8] Although they were able to show quicker healing, earlier resolution of acute pain, and improved quality of life, the resolution of pain at 6 months was not statistically different than placebo. Recommendations for treating PHN include analgesics, gabapentin (starting much later in the disease course than in this study), amitriptyline, carbamazepine, topical lidocaine, topical capsaicin (over-the-counter), and topical triethanolamine salicylate. The FDA recently approved a topical 8% patch formulation of capsaicin (Qutenza) for local treatment of PHN. It is available only by prescription.

Intervention should always balance benefit and harms. Although valacyclovir is FDA-approved for the treatment of HZ and gabapentin for the treatment of PHN, I cannot recommend the early use of both to prevent PHN, based on this study. On the other hand, what harm might befall your patient? Elderly patients are more likely to suffer central nervous system adverse effects (dizziness and drowsiness) from these drugs. If you can reduce that risk, it may be worth a month's trial. ■

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Aspirin for Primary Prevention

ABSTRACT & COMMENTARY

By Michael H. Crawford, MD

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

This article originally appeared in the August issue of Clinical Cardiology Alert. *At that time it was peer reviewed by Ethan Weiss, MD, Associate Professor of Medicine, Division of Cardiology, University of California, San Francisco, CA. Dr. Weiss is an advisory board member for Bionovo.*

Source: Bartolucci AA, et al. Meta-analysis of multiple primary prevention trials of cardiovascular events using aspirin. *Am J Cardiol* 2011;107:1796-1801.

THE USE OF ASPIRIN FOR THE PRIMARY PREVENTION OF CARdiovascular (CV) disease remains controversial. In this publication, Bartolucci updates his 2006 meta-analysis by adding three new trials to the six previous ones. Since aspirin may have different effects on different CV diseases, the data were classified into several outcomes of interest compared in almost 51,000 subjects on aspirin and more than 49,000 on placebo. Individually, only two trials showed a significant decrease in CV mortality, but each trial was significant for at least one CV endpoint. For example, the Women's Health Study (WHS) was significant for stroke reduction only. The nine-trial combined results showed a decreased risk of myocardial infarction (MI; $P = 0.042$) and total CV events ($P = 0.001$, CV death, MI, and stroke). There was significant heterogeneity across trials in total coronary heart disease ([CHD] MI and death due to CHD $P = 0.001$ and MI $P = 0.004$). The combined hazard ratios for six different endpoints ranged from 0.813 to 0.956 in favor of aspirin for risk reductions of 4.4% to 18.7%. Only nonfatal CHD events, total CHD, and the combined endpoint of CV death, MI, and stroke were reduced > 10%. Stroke reduction was 8.1%, CHD mortality was 4.4%, and all-cause mortality was reduced 5.5%. The authors concluded that aspirin decreases the risk of CV events and MI, but not stroke, nor any CV cause of death or total mortality.

■ COMMENTARY

I hate it when healthy people ask me if they should take an aspirin a day because I do not have the answer to this simple question. Thus, I read this latest meta-analysis with high expectations that I would get the answer. So imagine my disappointment that this question still does not have a clear answer. This analysis of nine primary prevention trials included two new trials that studied diabetics without symptomatic vascular disease. The inclusion of diabetics could mean more events and a greater chance to see differences in these higher risk subjects. Disappointingly these studies in diabetics showed that some outcomes were worse on aspirin, including CHD mortality.

The overall analysis showed a reduction in coronary events, but not stroke. No mortality endpoint was significantly reduced. This has always bothered me — how can an event be reduced, but the mortality from it not? Are such results important? Also in this analysis, the percent reductions in outcomes varied from 4% to 18%. When you weigh in the risk of gastrointestinal bleeding, even the authors admit that the net benefit is uncertain.

Despite including nine trials, almost 60% of the subjects came from the WHS and the Hypertension Optimal Treatment (HOT) study. The WHS was only positive for a reduction in stroke in older women. HOT showed reduced events, but not mortality, and overall was closer to the results of the meta-analysis. Based on these two studies, it has been concluded that aspirin prevents stroke in women and heart attack in men, but it is not as simple as that in the overall results of this meta-analysis.

What this analysis does not provide is any breakdown of the results by age, sex, or risk profile of the subjects, nor the dose of aspirin. If we are going to individualize therapy, we

need to know these variables. Since there is no strong message from this analysis, therapy will need to be individualized. Also, most of these studies included only middle-aged or older subjects, but at what age do we start recommending aspirin? Based on many studies, aspirin is clearly indicated for secondary prevention in all vascular disease patients, and probably for those who probably have vascular disease based on their risk profile, but not necessarily diabetics unless they have a high-risk profile. For the true primary prevention group of low-to-intermediate risk subjects, aspirin prophylaxis probably should not be considered until age 45 in men and 55 in women since vascular events are unusual before those ages and the risks of bleeding would outweigh the potential benefit. In the older subjects at low risk — I leave the decision to the subject and if they choose to take aspirin — I recommend 81 mg of the enteric coated type. You can make a better case for the intermediate-risk patient, but we do not know if just vigorously controlling their risk factors would be enough. This type of comparative effectiveness study of aggressive risk factor control plus or minus aspirin has not, and probably will not be done, so we can only speculate on the results. ■

Pharmacology Update

Emtricitabine/Rilpivirine/ Tenofovir Disoproxil Fumarate Tablets (Complera™)

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

Dr. Elliott is Chair, Formulary Committee, Northern California Kaiser Permanente; and Assistant 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 relationship to this field of study.

The FDA has approved a second three-drug fixed combination for the treatment of HIV-1 infections. This combination contains two nucleoside analog HIV-1 reverse transcriptase inhibitors (emtricitabine and tenofovir) and a non-nucleoside reverse transcriptase inhibitor (NNRTI; rilpivirine). This differs from the first fixed combination, Atripla, which contains efavirenz as the NNRTI. The new fixed combination is marketed by Gilead Sciences as Complera.

Indications

Emtricitabine/rilpivirine/tenofovir (FTC/TDF/rilpivirine) is indicated for the treatment of HIV-1 infection in treatment-naïve adults.[1]

Dosage

The recommended dose is one taken once daily with a meal. Each tablet contains 200 mg of emtricitabine, 25 mg of rilpivirine, and 300 mg of tenofovir disoproxil fumarate.

Potential Advantages

Rilpivirine appears to be better tolerated than efavirenz with fewer grade 2-4 adverse events and a lower frequency of discontinuation of therapy due to adverse events.[1-3]

Potential Disadvantages

In patients with baseline HIV-1 viral load greater than 100,000 copies/mL, the rate of virologic failure is higher with rilpivirine compared to efavirenz.[1] These virologic failures have a higher rate of overall treatment resistance and cross-resistance to the NNRTI class. FTC/TDF/rilpivirine is not recommended for patients with creatinine clearance below 50 mL per minute.[1] CYP3A4 inducers or inhibitors may affect the plasma level of rilpivirine. Drugs that increase gastric pH (i.e., antacid, H-2 antagonist, PPI) may decrease levels of rilpivirine.

Comments

FTC/TDF/rilpivirine provides a complete regimen for the treatment of HIV-1 infections. The efficacy of ERT was shown in two international randomized, double-blind, double-dummy, Phase 3 studies of identical design. Treatment-naïve subjects with a baseline plasma HIV-1 viral load of 5000 copies or greater were randomized to efavirenz (600 mg daily) or rilpivirine (25 mg daily) in combination with a background regimen. In one study, ECHO (n = 690), the background regimens were emtricitabine and tenofovir and the other, THRIVE (n = 678); the investigators had the option of emtricitabine/tenofovir, lamivudine/zidovudine, or abacavir/lamivudine.[1-3] The primary outcome was noninferiority of rilpivirine to efavirenz in terms of a confirmed virological response at week 48 with non-inferiority defined as a margin of 12% (i.e., lower limit of a two-sided 95% confidence interval [CI] is greater than -12%). Secondary outcomes included, but were not limited to, non-inferiority with a 10% margin, change in CD4 cell count, and safety and tolerability. Response rates from ECHO were 83% for both rilpivirine and efavirenz and 86% and 82% for THRIVE. The lower 95% CI were -5.9% and -1.7%, respectively, meeting the criteria for non-inferiority at the -12% and -10% margin. In comparison of the same background regimen (ECHO), virological failure was higher for rilpivirine (11% vs 4% in ECHO) and appeared to be associated with baseline HIV-1 RNA viral load. In patients with viral load of

500,000 copies/mL, response rates were 62% for rilpivirine compared to 81% for efavirenz compared to 90% vs 83% in patients with viral load of 100,000 copies/mL or less.[2] Grade 2-4 adverse events were lower for rilpivirine, 16% compared to 31% for both ECHO and THRIVE. Rash (8% vs 2%), dizziness (7% vs 1%), and abnormal dreams (5% vs 1%) were more common with efavirenz.[2] Increases in plasma lipids were lower with rilpivirine.

Clinical Implications

FTC/TDF/rilpivirine is the second three-drug fixed combination to be approved and provides an alternative to atripla. These provide a complete regimen, reduces pill burden, and may improve adherence. Rilpivirine appears to be better tolerated than efavirenz but may be less effective in patients with high viral load (100,000 copies/mL). Atripla is one of the initial regimens recommended by the Health and Human Services Panel for treatment-naïve patients.[4] Others are ritonavir-boosted atazanavir + tenofovir/emtricitabine, raltegravir + tenofovir/emtricitabine, and ritonavir-boosted darunavir + tenofovir/emtricitabine. ■

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CME Objectives

Upon completion of this educational activity, participants should be able to:

- describe new findings in the differential diagnosis and treatment of various diseases;
- describe the advantages, disadvantages and controversies surrounding the latest advances in the diagnosis and treatment of disease;
- identify cost-effective treatment regimens;
- explain the advantages and disadvantages of new disease screening procedures.

CME Instructions

To earn credit for this activity, follow these instructions:

1. Read and study the activity, using the provided references for further research.
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5. Once the completed evaluation is received, a credit letter will be e-mailed to you instantly. You will no longer have to wait to receive your credit letter! ■

CME Questions

1. **Which one of the following statements is true?**
   a. The blinded placebo has a powerful effect on the common cold reducing the duration of the illness from 7 to 4 days
   b. An open-label use of echinacea has a much stronger effect than a blinded use of the supplement
   c. A belief in the effectiveness of echinacea is a powerful force for reducing the duration and severity of the common cold.
   d. All of the above

2. **Your 70-year-old patient presents with a clinical diagnosis of acute herpes zoster. The rash appeared yesterday. He rates the pain as 8 out of 10. Which statement about the combination use of valacyclovir and gabapentin is true?**
   a. There is about a 10% chance that he will still have pain at 6 months.
   b. Valacyclovir is approved for use in treating postherpetic neuralgia.
   c. Gabapentin is approved for use in treating acute herpes zoster.
   d. Patients his age are less likely to develop postherpetic neuralgia than younger patients.
   e. Patients with severe pain like his are more likely to have resolution of the pain than patients with mild pain.

Clinical Briefs

By Louis Kuritzky, MD, Clinical Assistant Professor, University of Florida, Gainesville

Dr. Kuritzky is an advisor for Endo, Kowa, Pricara, and Takeda.

Encouraging News About Lung Cancer Screening Benefits

Source: National Lung Screening Trial Research Team. Reduced lung-cancer mortality with low-dose computed tomographic screening. *N Engl J Med* 2011; 365:395-409.

Screening for lung cancer by means of chest X-ray (CXR) does not reduce mortality, even with the addition of sputum cytology. Because low-dose helical CT (LDCT) detects much smaller, earlier lesions, the National Cancer Institute initiated a clinical trial in 2002 to determine whether LDCT screening, as compared to CXR, could reduce lung cancer (LCa) mortality.

Criteria for inclusion included at least a 30-year pack history of cigarette smoking, but if patients had signs of potential current LCa (e.g., hemoptysis, unexplained weight loss), they were not included. Study subjects were randomized to LDCT (n = 26,722) or CXR (n = 26,732) and underwent imaging at baseline, 1 year later, and 2 years later. Over the course of three screenings, 39% in the LDCT group and 16% in the CXR group had positive findings, of these more than 94% were false-positive — i.e., they were not LCa.

Evaluation of positive screening led to the diagnosis of LCa in 1060 of the LDCT group and 941 in the CXR group, so LDCT successfully identified about 13% more LCa. At 6 years of follow-up, LCa-related mortality was 20% lower in the LDCT group than the CXR group, and all-cause mortality was also 6.7% lower (both were statistically significant). Before widespread adoption of LDCT occurs, it has been suggested that cost-effectiveness analyses be performed, especially since the absolute risk reduction in mortality within the total study population was very small (1.31% vs 1.62%). ■

Comparing Metrics for Identification of Prediabetes

Source: Heianza Y, et al. HbA1c 5·7-6·4% and impaired fasting plasma glucose for diagnosis of prediabetes and risk of progression to diabetes in Japan (TOPICS 3): A longitudinal cohort study. *Lancet* 2011; 378:147-155.

Since more than half of newly diagnosed diabetics have one or more of the complications of diabetes already existing by the time of diagnosis, it is clear that we must strive for earlier identification of persons destined to develop diabetes and try to forestall or prevent it. The category "prediabetes" includes persons with impaired fasting glucose ([IFG] = 100-125 mg/dL), impaired glucose tolerance ([IGT] 2-hr PPG = 140-199), or elevated A1c (A1c = 5.7-6.4). In most prior clinical trials of diabetes prevention, inclusion required the presence of IGT, with or without IFG, since IGT was felt to be a better predictor of likelihood to progress from prediabetes to diabetes. In clinical practice, very few prediabetes patients are identified by glucose tolerance testing because of the cumbersome nature of the testing. Because utilization of A1c has only recently been condoned as a diagnostic tool for prediabetes, it is worthwhile to peruse the results of an observational trial that followed adults (n = 6241) without diabetes at baseline and compared the predictive capacity of A1c and IFG.

Over 4.7 years of follow-up, more than twice as many individuals developed IFG (n = 1680) than increased A1c (n = -822), and of course some (n = 410) developed both. The predictive capacity of A1c alone was quite similar to IFG alone, but since the two groups have only modest overlap, A1c and IFG actually define somewhat different populations destined to become diabetic. Hence, the authors suggest that using both measurements at the same time is necessary to capture the largest segment of persons with prediabetes. ■

Treatment of Depression in Patients with Dementia

Source: Banerjee S, et al. Sertraline or mirtazapine for depression in dementia (HTA-SADD): A randomised, multicentre, double-blind, placebo-controlled trial. *Lancet* 2011;378:403-411.

The evidence base supporting efficacy of antidepressant pharmacotherapy in patients with dementia is sparse and inconsistent. Banerjee et al performed a double-blind, randomized, placebo-controlled trial in patients with dementia and depression to assess the effects of two commonly used antidepressants: sertraline and mirtazapine.

Study subjects were randomized to sertraline 150 mg/d (n = 107), mirtazapine 45 mg/d (n = 108), or placebo (n = 151) with no other changes in their medical regimen. Each active antidepressant was initiated at a low dose and titrated within 4 weeks to a higher dose if depression scores had not substantially improved. Outcomes were measured with the Cornell Scale for Depression in Dementia (CSDD).

At the conclusion of the trial, neither sertraline nor mirtazapine provided improvements in CSDD scores greater than placebo, but side effects were more frequent in the active treatment arms. Although the authors do not provide any specific suggestions about what treatments might be preferred (beyond counseling) in the face of these disappointing results, their outcomes suggest reconsideration of preferred treatment for patients with depression associated with dementia. ■

Is the AV Block Complete?

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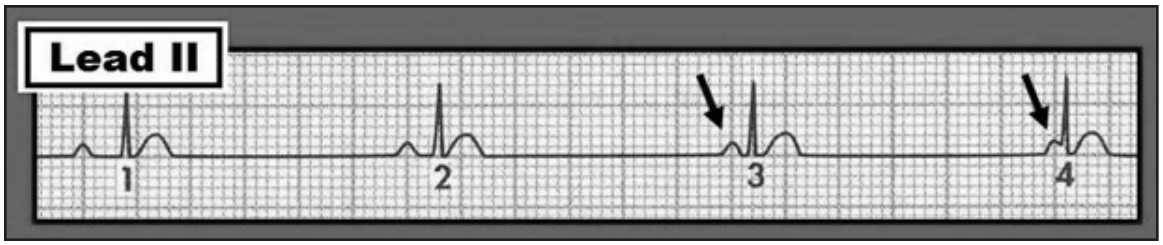

Scenario: Interpret the rhythm strip shown above. Does it represent complete (3rd degree) AV Block? How would you proceed clinically?

Interpretation: The ventricular rhythm in the Figure is regular at a rate just over 50/minute (since the R-R interval is slightly less than 6 large boxes in duration). The QRS complex is narrow, indicating a supraventricular etiology. P waves are present — however, they are not consistently conducting. Instead, the PR interval is changing. The PR interval preceding beats #3 and #4 (arrows) is clearly *too* short to conduct.

In the ECG Review from July 15, 2011 (*see page 104*), we defined the three degrees of AV block as follows:

• 1st degree AV block — in which *all* atrial impulses are conducted to the ventricles, albeit with delay (so that the PR interval exceeds 0.20 second).

• 2nd degree AV block — in which *some* (but not all) atrial impulses are conducted to the ventricles.

• 3rd degree (or "complete") AV block — in which *none* of the atrial impulses are conducted to the ventricles, despite having adequate opportunity for conduction to occur.

The *key* to the diagnosis of complete AV block is in the last part of the definition: No atrial impulses are conducted to the ventricles "despite having adequate opportunity for conduction to occur." Although beats #3 and #4 in the Figure (and possibly also beat #2) are *not* conducted to the ventricles — *none* of these beats has a "chance" to conduct, since the PR interval is simply too short. Thus, we have no idea if *any* degree of AV block is present — since we cannot tell from this tracing if P waves could conduct were they given the opportunity to do so. We therefore interpret this tracing as showing "AV dissociation," since some P waves are *unrelated* to the QRS complexes that follow them. AV dissociation is never a "diagnosis" per se. Instead, it is the result of the underlying rhythm on the tracing. In this case — the underlying rhythm is sinus bradycardia at a rate of 50/minute (the P-P interval is precisely 6 large boxes in duration for each of the P waves on this tracing). AV dissociation occurs by "default." That is, due to the relatively slow sinus rate, a nodal rhythm (at ~52/minute) takes over. This rhythm variant is not uncommonly seen in otherwise healthy, young adult individuals. It may well be that there is *no* degree of AV block present, and that normal conduction will resume whenever the sinus node speeds up to a normal rate. Diagnosis of 3rd degree AV block should be reserved for when no P waves conduct despite having adequate opportunity to do so. ■

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