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Internal Medicine

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ABSTRACT & COMMENTARY

How Much More Physical Activity Helps Patients Avoid Chronic Diseases?

By Seema Gupta, MD, MSPH

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

SYNOPSIS: Higher levels of total physical activity are strongly associated with lower risk of five common chronic diseases: breast and bowel cancer, diabetes, heart disease, and stroke.

SOURCE: Kyu HH, Bachman VF, Alexander LT, et al. Physical activity and risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events: Systematic review and dose-response meta-analysis for the Global Burden of Disease Study 2013. *BMJ* 2016 Aug 9;354:i3857.

Physical activity may provide a protective effect against several chronic conditions as well as all-cause mortality. The amount of time Americans spend engaging in sedentary activities, such as watching television or playing video games, is steadily rising. Such habits have been independently associated with increased risks of several chronic conditions and mortality.[1]

The World Health Organization (WHO) recommends at least 600 metabolic equivalent (MET) minutes of total activity per week for health benefits. For example, a patient could engage in about 150 minutes per week of brisk walking or 75 minutes per week of running.[2] One MET equals the resting metabolic rate of approximately 3.5 mL O_2/kg/min, and represents the approximate rate of oxygen consumption of a seated adult at rest. Although the beneficial effects of exercise appear to be dose-dependent, there is a paucity of studies that have systematically quantified the dose-response relations between physical activity and chronic disease endpoints. In the existing literature, often the focus is on studying a single activity domain, such as leisure

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time activity, and its effect on the chronic disease in question.[3,4] Rarely is that true for a patient who engages in multiple daily physical activities. However, no study to date has been able to quantify the total physical activity required to have an effect on chronic diseases in a dose-response manner.

Kyu et al quantified the dose-response associations between total physical activity and the risk of breast cancer, colon cancer, diabetes, ischemic heart disease, and ischemic stroke events. They analyzed the results of 174 studies published between 1980 and 2016, examining the associations between total physical activity and at least one of these five chronic diseases.

The researchers found that a higher level of total weekly physical activity was associated with a lower risk of all five conditions. Most health gains occurred at a total activity level of 3,000-4,000 MET minutes per week, with diminishing returns at higher activity levels. They found that an increase from the currently recommended level of 600 MET minutes per week to 3,600 MET minutes per week reduced the risk by an additional 19%. Furthermore, the researchers found that compared with less active individuals (total activity < 600 MET minutes per week), the risk reduction for those in the highly active category (≥ 8,000 MET minutes per week) was 14% (relative risk [RR], 0.863; 95% confidence interval [CI], 0.829-0.900) for breast cancer; 21% (RR, 0.789; 95% CI, 0.735-0.850) for colon cancer; 28% (RR, 0.722; 95% CI, 0.678-0.768) for diabetes; 25% (RR, 0.754; 95% CI, 0.704-0.809) for ischemic heart disease; and 26% (RR, 0.736; 95% CI, 0.659-0.811) for ischemic stroke. The authors concluded that individuals who can achieve total physical activity levels several times higher than the currently recommended minimum level experience a significant reduction in the risk of the five diseases under study.

■ COMMENTARY

We know that physical activity is good for health, but clinicians are uncertain about how much physicial activity produces positive outcomes and to what degree. In the past, while some studies have evaluated the physical activity as a whole, others have concentrated on specific types of activity. The study by Kyu et al represents a significant advance in our understanding of the significance of total physical activity as well as its dose-response effect on a set of chronic illnesses.

As the results suggest, the total physical activity perhaps should be several times higher than the current recommended minimum level of 600 MET minutes a week to potentially achieve much larger risk reductions of these diseases. With the total physical activity concept, it may not be very difficult to achieve such a task. For example, a patient can achieve 3,000 MET minutes a week by incorporating different types of physical activity into his or her daily routine, such as climbing stairs for 10 minutes, vacuuming for 15 minutes, gardening for 20 minutes, running for 20 minutes, and walking or cycling for 25 minutes.

Although this meta-analysis was based on observational studies, and therefore may not prove a relationship between the amount and/or type of physical activity and a lowering of the risk of chronic disease, it makes sense for clinicians to prescribe prevention in the form of total physical activity. With an aging population, that does not have to be just exercise but a host of activities for patients that are easy to perform and that can become part of their lifestyle. ■

REFERENCES

1. Ekelund U, Steene-Johannessen J, Brown WJ, et al. Does physical activity attenuate, or even eliminate, the detrimental association of sitting time with mortality? A harmonised meta-analysis of data from more than 1 million men and women. *Lancet* 2016 Jul 27. pii: S0140-6736(16)30370-30371.
2. U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. Physical activity guidelines for Americans. Available at: http://bit.ly/2bXF6yT. Accessed Sept. 7, 2016.
3. Aune D, Norat T, Leitzmann M, et al. Physical activity and the risk of type 2 diabetes: A systematic review and dose-response meta-analysis. *Eur J Epidemiol* 2015;30:529-542.
4. Sattelmair J, Pertman J, Ding EL, et al. Dose response between physical activity and risk of coronary heart disease: A meta-analysis. *Circulation* 2011;124:789-795.

ABSTRACT & COMMENTARY

Screening for Coronary Artery Disease Is Underused in Heart Failure

By Van Selby, MD

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

SYNOPSIS: In a large retrospective cohort of patients hospitalized for new-onset heart failure, the majority did not receive testing for ischemic heart disease.

SOURCES: Doshi D, Ben-Yehuda O, Bonafede M, et al. Underutilization of coronary artery disease testing among patients hospitalized with new-onset heart failure. *J Am Coll Cardiol* 2016;68:450-458.

Coronary artery disease (CAD) is the most common cause of heart failure (HF). Current practice guidelines call for screening for CAD in patients with newly diagnosed HF. However, few researchers have evaluated how often clinicians perform diagnostic testing for CAD on patients hospitalized with newly diagnosed HF.

Doshi et al analyzed a large commercial administrative claims database, supplemented by Medicare data. They evaluated the frequency of diagnostic testing for CAD, both during the index hospitalization for new-onset HF and within 90 days of hospitalization. Between 2010 and 2013, the authors identified 67,691 patients.

Overall, 17.5% of patients underwent any testing for ischemic CAD during the index hospitalization, and 27% were evaluated for CAD within 90 days. The most common evaluation method was stress testing, followed by coronary angiography. In a multivariable analysis, predictors of undergoing noninvasive testing for CAD included baseline CAD (odds ratio [OR], 1.25; $P < 0.001$), hypertension, hyperlipidemia, and reduced ejection fraction. Patients who were > 70 years of age and those presenting with prior stroke, peripheral arterial disease, prior arrhythmia, renal disease, or a prior workup for CAD were less likely to receive noninvasive testing for CAD.

Only 2% and 4.3% of patients underwent coronary revascularization during the index hospitalization and at 90 days, respectively. Baseline CAD (OR, 9.27; $P < 0.001$), male sex, diabetes, and smoking all were associated with greater odds of coronary revascularization, and percutaneous coronary intervention was used more commonly than coronary artery bypass grafting. The authors concluded that diagnostic testing for ischemic CAD is underutilized significantly among patients hospitalized for new-onset HF.

■ COMMENTARY

Not every patient hospitalized for new HF requires evaluation for CAD within 90 days, and the exact percentage of patients who should be evaluated is unknown. However, considering CAD is the most common cause of HF and present in more than half of patients with HF, the rate of CAD testing reported in this study (27% of all patients were evaluated within 90 days) is surprisingly low and suggests, as the authors concluded, that diagnostic testing for CAD is underutilized significantly in this population. Part of the explanation for low use of ischemic evaluation in new HF may be a perceived lack of evidence showing clear benefit of revascularization in patients presenting with HF and CAD. Perhaps because of this lack of data, the most recent HF guidelines from the American College of Cardiology/American Heart Association only make a class IIa recommendation (meaning it is reasonable) to evaluate for CAD in the diagnostic evaluation of new HF. The recent publication of 10-year follow-up from STICHES, showing a mortality benefit associated with coronary artery bypass grafting in patients with CAD and systolic HF, may strengthen the argument for CAD testing. Regardless of the benefits associated with revascularization, identification of CAD also may guide medical therapy of a given patient.

When evaluating findings of large retrospective cohort studies, it is important to acknowledge limitations. Analyses of insurance claims databases depend on accurate coding, and it is possible that diagnostic testing for CAD was not always coded properly. Furthermore, complete clinical information is not available for these patients — some may have had a contraindication to diagnostic testing or other explanation for why no one performed tests. Despite these limitations, given the size of the cohort and the magnitude of the findings, it appears the majority of eligible HF patients are not screened for CAD.

Identifying which HF patients will have underlying CAD is difficult based on clinical history of risk factors alone. Many will not have angina or other clear ischemic symptoms. Once CAD is identified, it may be difficult to determine whether it is the cause of a given patient's HF; however, this should not deter clinicians from testing. The authors suggested an increasingly cost-conscious medical environment, eager to minimize unnecessary diagnostic testing, is responsible for the low rates of CAD evaluation. By their estimate, clinicians miss 325,000 cases of CAD in patients with congestive HF every year due to underutilization of diagnostic testing. Whatever the reason, the rates of CAD testing reported in this study would strike most cardiologists as inappropriately low, and suggest those of us who evaluate and treat HF should consider screening for CAD more frequently in patients with newly diagnosed HF. ■

BRIEF REPORT

Calcium Supplementation and Increased Dementia Risk

By David Kiefer, MD

Clinical Assistant Professor, Department of Family Medicine, University of Wisconsin; Clinical Assistant Professor of Medicine, Arizona Center for Integrative Medicine, University of Arizona, Tucson

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

SYNOPSIS: In this five-year observational study, women who were taking calcium supplementation and who presented with pre-existing cerebrovascular disease were at higher risk of dementia than women not taking extra calcium.

SOURCE: Kern J, Kern S, Blennow K, et al. Calcium supplementation and risk of dementia in women with cerebrovascular disease. *Neurology* 2016; Aug 17. pii: 10.1212/WNL.0000000000003111.

Calcium is arguably the most commonly supplemented yet most controversial mineral with respect to what it does and does not do. People of all ages need it, some demographic groups more than others, but it is probably important to not ingest too much.[1] Despite the myriad clinical trials at one's disposal, clinicians may wonder how to encourage calcium intake so as to decrease the risk of osteoporosis and fractures, but at the same time avoid increased cancer risk (i.e., prostate) or cardiovascular disease.

The Kern et al study adds to the concern about unrestrained calcium supplementation. For five years, researchers followed 700 women 70-92 years of age and free of dementia. At baseline, and again at the conclusion of the study, the authors conducted extensive physical examination and neuropsychiatric studies. Additionally, researchers collected information about the use of calcium supplementation, including dose and form. In this cohort, 59 women (45 in the non-calcium group, and 14 who had been taking calcium) developed dementia over the course of the study. Also, 98 women reported taking supplemental calcium, putting them at higher risk of developing dementia (odds ratio [OR], 2.10; 95% confidence interval [CI], 1.01-4.37; $P = 0.046$), although this risk was barely significant when compared to the 602 women who were not taking calcium supplementation. The association was more significant ($P = 0.006$) for stroke-related dementia (OR, 4.40; CI, 1.54-12.61). Further, subgroup analyses revealed that the higher calcium-related dementia risk occurred in people who had suffered a previous stroke or who, on CT (447 of the 700 patients underwent this imaging at baseline), showed white matter changes, but not in those without these conditions. The authors described how the white matter changes are evidence of cerebrovascular disease.

Essentially, the higher risk of dementia in women taking calcium supplementation occurred mostly in those who already suffered from cerebrovascular disease. These results seem to be in line with some of the concerns about calcium supplementation, or elevated blood calcium levels, and vascular risk.[2] This trial showed the most pronounced association with vascular-type dementia, and, as mentioned above, the calcium risk added to pre-existing risk. An observational study like this allows associations to be demonstrated but any cause-effects are merely inferred. Besides, the number of dementia cases (14 in the calcium supplementation group) was very small, possibly compromising the statistical power and accuracy of the findings. Clearly, a well-designed, randomized, controlled trial is indicated to corroborate the calcium-dementia connection. Until then, it would behoove clinicians to be cautious about the use of calcium supplementation in women with a history of cerebrovascular disease because of these concerns about dementia risk. ■

REFERENCES

1. Ross AC, Manson JE, Abrams SA, et al. The 2011 Report on

Dietary Reference Intakes for Calcium and Vitamin D from the Institute of Medicine: What Clinicians Need to Know. *J Clin Endocrinol Metab* 2011;96:53-58.
2. Wang X, Chen H, Ouyang Y, et al. Dietary calcium intake and mortality risk from cardiovascular disease and all causes: A meta-analysis of prospective cohort studies. *BMC Med* 2014;12:158. doi: 10.1186/s12916-014-0158-6.

PHARMACOLOGY UPDATE

Etanercept-szzs Injection (Erelzi)

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 a biosimilar to the tumor necrosis factor (TNF-alpha) blocker etanercept (Enbrel). 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.[1] Etanercept-szzs is the third biosimilar drug to be approved in the United States. It is marketed as Erelzi.

INDICATIONS

Etanercept-szzs is indicated for moderate to severe active rheumatoid arthritis (RA), moderate to severe active polyarticular juvenile idiopathic arthritis (JIA), psoriatic arthritis (PsA), active ankylosing spondylitis (AS), and chronic moderate to severe plaque psoriasis (PsO).[2]

DOSAGE

The recommended dose for RA and PsA is 50 mg once weekly with or without methotrexate; for AS, 50 mg once weekly; for PsO, 50 mg twice weekly for three months, then 50 mg once weekly; and JIA (> 63 kg), 0.8 mg/kg weekly, with a maximum of 50 mg per week.[2] Etanercept-szzs is available as 25 mg/0.5 mL and 50 mg/mL single-dose prefilled syringe and 50 mg/mL single-dose prefilled Sensoready Pen.

POTENTIAL ADVANTAGES

Etanercept-szzs provides an alternative to etanercept (Enbrel).

POTENTIAL DISADVANTAGES

Etanercept-szzs currently is not designated as interchangeable to Enbrel, which means it cannot be substituted without provider approval.

COMMENTS

Etanercept-szzs was approved based on elements of biosimilarity. These include structural and functional characterization, animal study data, human pharmacokinetic and pharmacodynamic data, clinical immunogenicity, and other safety and effectiveness data.[3] In vitro tests showed that etanercept-szzs and etanercept had comparable binding affinities to TNF-alpha, C1q complement, and complete panel of Fc receptors.[4] There was sufficient data from the clinical studies section for the prescribing information to be the same for etanercept-szzs and etanercept. To be labeled as interchangeable, the biosimilar product is expected to produce the same clinical result as the reference product in any given patient. Additionally, if a product is to be administered to a patient more than once, the risk in terms of safety and effectiveness of alternating or switching between the interchangeable and the reference product is not greater than the risk of using the reference product without alternating or switching.[5]

CLINICAL IMPLICATIONS

Etanercept-szzs is the first biosimilar to Enbrel approved in the United States. It joins infliximab-dyyb, a biosimilar to Remicade, as commonly used biologics for chronic inflammatory diseases. Neither was approved as an interchangeable product, thus neither can be substituted for the reference drug without provider approval. Pricing for etanercept-szzs was not available at the time of this review. ■

REFERENCES

1. U.S. Department of Health and Human Services. Biosimilars: Questions and Answers Regarding Implementation of the Biologics Price Competition and Innovation Act of 2009. Available at: http://bit.ly/1JT8WdH. Accessed Sept. 9, 2016.
2. Erelzi Prescribing Information. Sandoz Inc. August 2016.
3. FDA News Release. FDA approves Erelzi, a biosimilar to Enbrel. Available at: http://bit.ly/2c6iMRy. Accessed Sept. 9, 2016.
4. Hofmann HP, Kronthaler U, Fritsch C, et al. Characterization and non-clinical assessment of the proposed etanercept biosimilar GP2015 with originator etanercept (Enbrel). *Expert Opin Biol Ther* 2016;16:1185-1195.
5. FDA. Information for Consumers (Biosimilars). Available at: http://bit.ly/1rvPtuj. Accessed Sept. 14, 2016.

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CME QUESTIONS

1. **Researchers found that an increase from the currently recommended level of 600 metabolic equivalent minutes per week to 3,600 metabolic equivalent minutes per week reduced the risk of chronic diseases by an additional:**
   a. 5%.
   b. 12%.
   c. 19%.
   d. 24%.

2. **In a large insurance survey study, approximately what proportion of newly diagnosed heart failure patients were evaluated for coronary artery disease within 90 days?**
   a. 25%
   b. 50%
   c. 75%
   d. 95%

3. **In the study about dementia risk and calcium supplementation, which of the following is true?**
   a. Calcium supplementation lowers dementia risk.
   b. There is a marked increase in risk of dementia if supplemental calcium is taken, regardless of cerebrovascular disease status.
   c. Men, but not women, benefitted from calcium supplementation.
   d. Women who had a prior stroke or who had white matter changes on CT scan were at particular risk of increase dementia with calcium supplementation.

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.

[IN FUTURE ISSUES]

Efficacy and Safety of Statin Therapy

The Growing Threat of Pyelonephritis Caused by Antibiotic-resistant *E. coli*

Clinical Briefs

By Louis Kuritzky, MD

Efficacy of Water Aerobics for Overweight and Obese Hypertensive Women

SOURCE: Cunha R, Arsa G, Neves EB, et al. Water aerobics is followed by short-time and immediate systolic blood pressure reduction in overweight and obese hypertensive women. *J Am Soc Hypertens* 2016;10:570-577.

Clinicians sometimes are concerned about the effect of exercise on blood pressure in hypertensive patients, primarily because of a well-recognized post-exercise hypotension phenomenon that can occur. Typically, hypertensive patients experience greater degrees of hypotension than normotensive patients. There is a paucity of evidence about whether hypotension occurs with similar frequency, intensity, and duration after water aerobics as it does during exercise on land. An additional attractive feature of water aerobics is that overweight and obese subjects sustain less joint stress. Injuries associated with water aerobics are much less common than during land exercise.

In a small crossover study of overweight and obese hypertensive women (n = 18), participants were randomized to either water aerobics (performed at 70-75% of predicted maximum heart rate for 45 minutes) or control (sedentary pool-side participation). Blood pressure was measured at 10-minute intervals three times after the 45-minute interval of exercise (or sedentary activity). Participants then crossed over so that the previously sedentary group performed aerobic exercise, and vice versa.

In study subjects, post-exercise changes did not occur in diastolic blood pressure. Systolic blood pressure changes were small (1-3 mmHg decline) and not of clinical relevance. Clinicians who provide exercise advice to overweight and obese hypertensive patients should find some reassurance about the safety of aerobic exercise in this population. ■

Topicals for Atopic Dermatitis: Calcineurin Inhibitors vs. Corticosteroids

SOURCE: Broeders J, Ahmed Ali U, Fischer G. Systematic review and meta-analysis of randomized clinical trials (RCTs) comparing topical calcineurin inhibitors with topical corticosteroids for atopic dermatitis: A 15-year experience. *J Am Acad Dermatol* 2016;75:410-419.

Atopic dermatitis is a chronic disorder, usually beginning in childhood, that causes significant burden to patients because of unsightly dermatitis, pruritus, and lichenification. Unfortunately, there is no cure for atopic dermatitis; rather, numerous interventions are available to provide reduction in symptoms, or at least temporary periods of remission.

The mainstay of pharmacotherapy for atopic dermatitis has been topical corticosteroids for more than three decades. Although highly successful, concern about local cutaneous toxicity of topical corticosteroids, as well as the potential for systemic effects on the hypothalamic-pituitary-adrenal axis when a high-potency topical corticosteroid is used, has prompted exploration of alternative treatments. Within the past decade, topical calcineurin inhibitors (i.e., pimecrolimus, tacrolimus) have demonstrated efficacy for atopic dermatitis. Because of largely hypothetical concerns about immune dysregulation that might occur with topical calcineurin inhibitors (TCI), current guidelines reserve TCI for second-tier treatment, such as steroid-refractory atopic dermatitis or patients intolerant of topical corticosteroids. Broeders et al compared the efficacy of topical corticosteroids with TCI through a meta-analysis of 12 trials that compared topical corticosteroids to TCI (n = 6,954) in adults and children presenting with atopic dermatitis. Overall efficacy of TCI was slightly greater, but it caused higher rates of non-serious adverse events. The authors concluded that topical corticosteroids should remain the first-line treatment for atopic dermatitis. ■

What's the Best Way to Remove a Tick?

SOURCE: Akin Belli A, Dervis E, Kar S, et al. Revisiting detachment techniques in human-biting ticks. *J Am Acad Dermatol* 2016;75:393-397.

Ticks transmit pathogens to victims around the globe. This particular data set was provided by a group of Turkish physicians, for whom the necessity to determine optimum tick removal technique was highlighted by a 2003 epidemic of tick-borne Crimean-Congo hemorrhagic fever that led to 300,000 tick-bite related admissions in one year.

Investigators studied four techniques — tweezers, freezing, lassoing, and card-detachment (a card with a narrow slit/channel into which a tick might be caught and removed) — among 160 patients presenting to the Dermatology Clinic at Haseki Training and Research Hospital (Istanbul). Except for the tweezer technique, all other methods were performed with commercial products specifically designed by the manufacturer to remove ticks.

There was great diversity in efficacy of tick removal, ranging from 0% (freezing), 7.5% (card-detachment technique), 47.5% (lassoing technique), and 82.5% (tweezers). The successful tweezer technique was simple: Grab the mouth parts, do not rotate, and pull off directly. ■

Internal Medicine [ALERT]

ECG Review

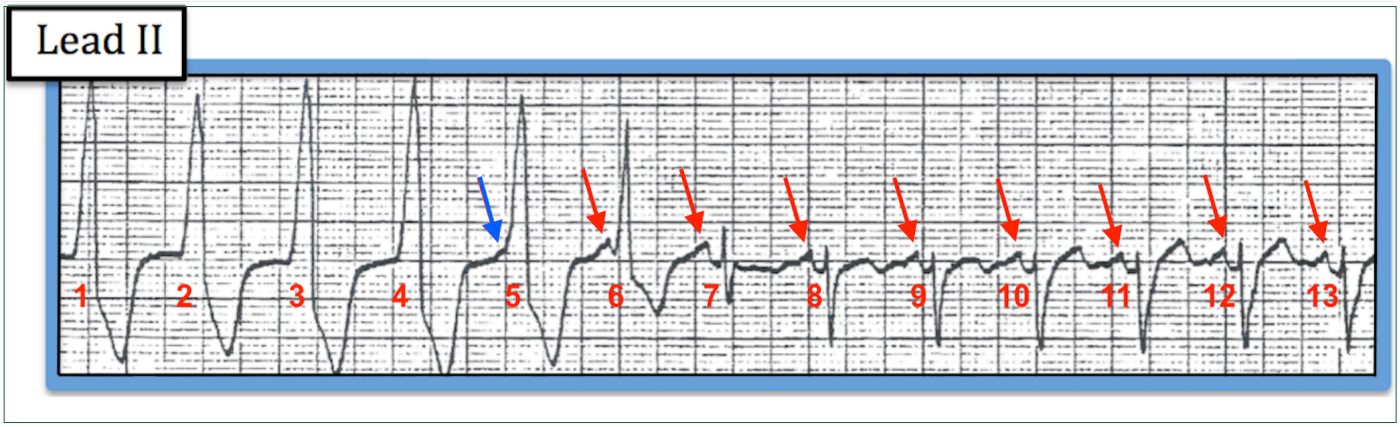
By Ken Grauer, MD

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.

What If Beats 5 and 8 Had Children?

How would you interpret the lead II rhythm strip shown in the figure below? How certain are you of your diagnosis? Are the P waves preceding beats six and seven conducting?



The easiest way to approach the interpretation of more challenging arrhythmias such as this one is to begin with the part of the tracing that is most evident and save the most difficult part for last. To do this, mentally block out the first seven beats on this tracing.

Beats 8 through 13 clearly show sinus tachycardia at a rate of 110/minute. Red arrows highlight upright sinus P waves in this lead II rhythm strip. Assessing the first five beats in this tracing also is straightforward. These beats show a regular, wide QRS rhythm at a rate between 100-105/minute, without preceding P waves. This suggests a ventricular etiology. Since the usual rate of an idioventricular escape rhythm is much slower (in the range of 20-40/minute), we describe the initial five beats as an accelerated idioventricular rhythm (AIVR).

This leaves us with the middle two beats (i.e., beats 6 and 7). Note that a P wave (red arrow) precedes beat 6. However, the PR interval preceding this beat is much shorter than the PR interval preceding each of the other sinus beats. This means that there simply was not enough time for the sinus impulse preceding beat 6 to complete its conduction pathway before "something else" must have happened. That "something else" must have come from the other direction, arising in the ventricles. Beat 6 is a fusion beat. Its QRS complex and T wave are intermediate in morphology between the much wider and taller morphology of ventricular beats (1 through 5), and the narrow, predominantly negative sinus-conducted beats (8 through 13).

Beat 7 also is a fusion beat. Since its preceding PR interval is longer and its QRS and T wave morphology more closely resembles the QRS and T wave morphology of subsequent sinus beats, fusion between near-simultaneous appearance of sinus and ventricular impulses occurred later in the cycle for beat seven.

Beat 5 actually is also a fusion beat. It, too, is preceded by a P wave (blue arrow highlighting the small bump deforming the initial part of the QRS). Note that beat 5 is not as tall (and its T wave is not as deep) as the first four beats in this tracing, which are pure ventricular beats.

Clinically, the reason recognition of fusion beats is important is that it proves the widened beats in a tracing must be of ventricular etiology. For a further discussion of this case, please visit: http://tinyurl.com/KG-Blog-128.