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Financial Disclosure:

Internal Medicine Alert's editor, Stephen Brunton, MD, is a consultant for Abbott, Amylin, Boehringer Ingelheim, Eli Lilly, Endo, Novartis, and Novo Nordisk. Peer reviewer Gerald Roberts, MD, reports no financial relationship to this field of study.

One Size Diet Does NOT Fit All

ABSTRACT & COMMENTARY

By Barbara A. Phillips, MD, MSPH

Professor of Medicine, University of Kentucky; Director, Sleep Disorders Center, Samaritan Hospital, Lexington

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

Synopsis: *A low-glycemic load diet is more likely to produce weight loss in obese young adults who have high insulin concentrations than is a low fat diet; it is also more likely to improve high-density lipoproteins (HDL) and triglycerides, regardless of insulin levels.*

Source: Ebbeling CB, et al. Effects of a low-glycemic load vs a low-fat diet in obese young adults. A randomized trial. *JAMA.* 2007;297:2092-2102.

BASED ON THE OBSERVATIONS THAT HIGH-GLYCEMIC FOOD intake induces more insulin secretion than low-glycemic food intake and that high insulin levels may stimulate appetite, these authors hypothesized that those people whose insulin response to a glycemic load was highest might have the most trouble losing weight on a high glycemic diet. (Glycemic load, by the way, is based somewhat on the carbohydrate availability of food. In general, complex starches have lower glycemic indices than do simple sugars, and fat and protein have very low glycemic indices.) To test their hypothesis, the investigators in this study recruited (through the media, including the internet) and randomized 73 obese young (average age 28 years) adults, mostly women. They do not report the mean Body Mass Index in this paper, but the mean percentage of body fat of this cohort was about 40%. Insulin secretion was assessed using an oral glucose tolerance test; the cut-point between high and low insulin secretors was 57.5 microunits/mL after 75 grams of oral glucose. The high and low insulin secretors were randomized to either a low-glycemic (40% carbohydrate, 25% protein, 35% fat) or a low-fat (55% carbohydrate, 25% protein, 20% fat) diet. Dietitians were heavily involved in this study, conducting education and follow-up throughout the study, and assessing adherence to assigned diet. The dietary instructions themselves were general (for example, those in the low glycemic arms were to eat nonstarchy vegetables, legumes, fruits, nuts seeds and oils, and to limit sweets and starches).

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Food intake was governed by simple instructions about satiety. The study lasted for 18 months, with the first 6 months being "intensive intervention," involving multiple workshops, counseling sessions, phone calls, and other educational efforts. Dietary glycemic load was calculated from food diaries. The investigators also collected data on physical activity, satisfaction with diet, and lipid levels. Because of drop-out and missing data, complete data analysis at 18 months is only available for 35 participants. For the entire cohort of 73 participants, weight loss did not differ between the two dietary groups. However, for the high-insulin secreting group, those who were randomized to the low-glycemic diet lost significantly more weight than those in the low fat diet (5.8 vs 1.2 Kg). In those who had low insulin levels after glucose challenge, there was no difference in weight loss between the 2 diets. Insulin response to glucose was not related to changes in lipid levels, but those in the low-glycemic diet had more improvement in high-density lipoproteins (HDL) and triglycerides, and those in the low-fat diet had more improvement in the low-density lipoproteins (LDL).

COMMENTARY

The lay press is full of information (and misinformation) about diets and weight loss, and often picks up on medical reports. The headline about this particular paper in *US News and World Report* exclaims, "Winning at losing. Your body's use of insulin may point to the right diet."[1] The article goes on to assert that it's time to rethink the one-size fits all approach to weight loss, and I agree. At the end of the day, caloric balance (out vs in) determines weight loss or gain. But the composition of those calories may profoundly affect appetite regulation. *The US News and World Report* article goes on to recommend getting a glucose tolerance test to determine if one is a high or low insulin secretor (expecting your physician, no doubt, to justify it to your insurance company), or to "tinker with your eating plan to see what works best." Because of concerns about effects of low-glycemic (which are generally higher in fat) diets on lipid levels, many clinicians have been reluctant to recommend such diets. It is noteworthy that in the current study, those in the low-glycemic diet had more improvement in HDL and triglycerides, and those in the low-fat diet had more improvement in the LDL.

A recent randomized trial[2] compared the Atkins (carbohydrate restriction), Zone (macronutrient balance), Weight Watchers (calorie restriction), and Ornish (fat restriction) diet groups. The main determinant of weight loss in this comparison was adherence to the diet, but only about half of the participants completed the trial. Notably, each diet significantly reduced the LDL/HDL cholesterol ratio. Previous work has demonstrated that low-carbohydrate (higher fat) diets can improve the metabolic syndrome,[3,4] and some work (larger than the current study) has shown that low glycemic (low carbohydrate, higher fat) diets may benefit the LDL cholesterol,[5,6] and reduce coronary heart disease.[7]

This paper helps to explain why some folks do well on a low-fat diet and others don't: those whose insulin response to a glycemic load is highest are less likely to be able to control their appetite (thus weight) in a low-fat diet. This phenotypic difference may help to explain some of the conflicting evidence about which diets "work."

Like many of our patients will, I Googled "glycemic index," and got over 1,200,000 hits. I went to the "Home of the Glycemic Index,"[8] and found this information about how to switch to a "this for that" approach—ie, swapping high GI carbs for low GI carbs. You don't need to count numbers or do any sort of mental arithmetic to make sure you are eating a healthy, low GI diet.

Internal Medicine Alert, ISSN 0195-315X, is published twice monthly by AHC Media LLC, 3525 Piedmont Road., NE, Building. 6, Suite 400, Atlanta, GA 30305.

SENIOR VICE PRESIDENT/GROUP PUBLISHER: Brenda Mooney.

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MANAGING EDITOR: Iris Young

GST Registration Number: R128870672.

Periodicals postage paid at Atlanta, GA.

POSTMASTER: Send address changes to ***Internal Medicine Alert***, P.O. Box 740059, Atlanta, GA 30374.

Back issues: $21. Missing issues will be fulfilled by Customer Service free of charge when contacted within one month of the missing issue's date.

This is an educational publication designed to present scientific information and opinion to health professionals, to stimulate thought, and further investigation. It does not provide advice regarding medical diagnosis or treatment for any individual case. It is not intended for use by the layman.

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This CME activity is intended for the internist/family physician. It is in effect for 36 months from the date of the publication.

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- Use breakfast cereals based on oats, barley and bran
- Use breads with whole grains, stone-ground flour, sour dough
- Reduce the amount of potatoes you eat
- Enjoy all other types of fruit and vegetables
- Use Basmati or Doongara rice
- Enjoy pasta, noodles, quinoa
- Eat plenty of salad vegetables with a vinaigrette dressing

I also found a very cogent (but much more sophisticated) explanation at Wikipedia.[9] Odds are, many of our patients have been to these places already.

The bottom line is that different diets might work better for different people. After decades of vilification, fat is back! ■

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Ethnic Variations in Normal Leukocyte and Neutrophil Values

ABSTRACT & COMMENTARY

By Mary Elina Ferris, MD

Clinical Associate Professor, University of Southern California

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

Synopsis: *Higher incidence of benign leukopenia from lower neutrophil counts is found in black persons compared to white in the United States, and Mexican-Americans and smokers have slightly higher routine counts.*

Source: Hsieh MM, et al. *Ann Intern Med.* 2007;146:486-492.

White blood cell counts were analyzed from 25,222 participants in the National Health and Nutritional Examination Survey (NHANES) conducted from 1999-2004 and were analyzed by age, sex, ethnicity and smoking status. The survey consists of an interview, examination and laboratory data. A complex sampling strategy, including oversampling of underrepresented groups to ensure accuracy, makes this representative of 253.2 million non-institutionalized U.S. residents. The threshold for neutropenia was defined as 1.5 x 10^9 cells/L as established by the National Cancer Institute.

Black participants had lower mean leukocyte and netrophil counts, with similar lymphocyte counts, compared to whites. Mexican-Americans had slightly higher counts of all types. Normal values for persons older than 18 years follow a bell-shaped curve for all ethnic groups, but blacks had a downward shift of approximately 1.0 x 10^9 for both leukocyte and neutrophil counts. The overall prevalence of neutropenia in blacks was 4.5%, compared to 0.8% for whites and 0.4% for Mexican-Americans. For black males the percentage was higher at 6.65% compared to 3.57% for black females. For 89% of the neutropenia in blacks, values were between 1.0-1.5 x 10^9.

Smokers in all ethnic groups had a higher overall mean leukocyte and neutrophil count than non-smokers, with an increase of 1.38 and 0.87 x 10^9 respectively, but blacks showed less of an increase than whites, and Mexican-Americans demonstrated the least effect.

■ COMMENTARY

Elimination of racial and ethnic disparities in health is a major national goal, and we need more information about normal variations to help us understand those disparities. Multiple past reports have documented asymp-

tomatic or benign reductions of neutrophil counts in several ethnic groups, eg, Bedouin Arabs, Ethiopian or Yemeni Jews, and persons of African descent. Hematologic analyses have shown normal bone marrow cellularity and normal subpopulations of other leukocyte types, without increased risk for infections.[1]

Early analysis of neutropenia in black children led to a belief that nutritional deficiency might be the cause, but multiple studies now over 3 decades and in several different locations lead more to a conclusion of "benign ethnic neutropenia." The extensive NHANES data in this study adds support for a genetic etiology since the finding is so widespread, and other variations were seen in the reverse direction in Mexican-Americans.

The effect of smoking on leukocyte and neutrophil counts is thought to be due to an inflammatory response, possibly contributing to increased atherosclerosis and bronchial disease. All of these significant differences in what we understand as "normal" should lead us to be much more aware of the individual when we interpret laboratory results.[2] ■

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Sequential Therapy vs Standard Triple-Drug Therapy for Helicobacter pylori Eradication

ABSTRACT & COMMENTARY

By Malcolm Robinson MD, FACP, FACG,

Emeritus Clinical Professor of Medicine, University of Oklahoma College of Medicine, Oklahoma City

Dr. Robinson reports no relationship to this field of study.

Synopsis: *Standard 10 day triple therapy for Helicobacter pylori may result in relatively low eradication rates. An alternative regimen of PPI plus amoxicillin for 5 days followed by PPI plus clarithromycin plus tinidazole for five days seems to provide significantly better H. pylori eradication.*

Source: Vaira Dino, et al. *Ann Inter Med.* 2007;1466:556-563.

THE SOMEWHAT INEXPLICABLE BUT ENORMOUS enthusiasm for the eradication of H. pylori has been discussed many times in *Internal Medicine Alert* in the medical literature, and in numerous lay publications. Although H. pylori infection certainly is associated with gastric and duodenal ulcers, MALT lymphomas, and gastric cancer, most of these disorders have progressively decreased in the United States. However, H. pylori remains classified by the World Health Organization as a Class I carcinogen. If eradication is to be accomplished (and it can be quite difficult), physicians should employ the regimen most likely to be successful. H. pylori infections are becoming resistant to metronidazole and clarithromycin. As a result, eradication rates attained with currently employed regiments are falling in most western countries.

A better therapeutic option is clearly needed. Several small studies have suggested that a novel 10-day sequential regimen could improve results. The present study evaluates this concept in 300 patients presenting with dyspepsia who were determined to have H. pylori infection by urea breath testing. Patients also were required to have at least 2 of the following tests positive for H. pylori: rapid urease testing on biopsy specimens, histological examination of the antral biopsies, and/or culture of the biopsy specimens. Patients had not previously received H. pylori treatment or any PPIs or H_2 receptor antagonists, bismuth preparations or antibiotics. No patients were taking ketoconazole or anticoagulants. Half received a standard 10-day regimen of pantoprazole 40 mg, 500 mg clarithromycin, and 1 gram of amoxicillin, all given twice daily. The other 150 patients received 40 mg of pantoprazole and 40 mg of amoxicillin twice daily for 5 days followed by 40 mg of pantoprazole, 500 mg of clarithromycin, and 500 mg of tinidazole twice daily for a second five day period. The conventional 10-day regimen produced 77% eradication of H. pylori vs 89% eradication in the group with the sequential regimen.

In the 143 patients evaluated in the "per protocol" analysis of the sequential group (completed all phases of therapy exactly as the protocol demanded), the eradication rate was 93% vs 79% in the 10-day triple therapy group (n = 146 per protocol). Rates of adverse events (some quite common) were equal in the 2 groups studied, but few patients withdrew (3 patients in the sequential group and 2 patients in those getting standard therapy). This study was performed in two large Italian hospitals, and the authors note that the results may or may not be applicable to H. pylori in other settings. The authors propose several plausible bacteriological explanations for the results, including the fact that tinidazole

was added to the sequential therapeutic mix (tinidazole is a drug similar to metronidazole).

COMMENTARY

This study suggests that there are likely to be a number of new approaches to the eradication of H. pylori including sequential regimens such as the one utilized in this study. It is probably too soon for us to adopt this approach until additional studies have been completed including clinical trials in North American settings and populations. As these authors comment, part of their success is undoubtedly due to the careful follow-up and detailed patient instructions intrinsic to a well run clinical trial. Similar results may not necessarily be attainable in the usual clinical practice setting, particularly in view of the annoying side effects present in all H. pylori eradication regimens (eg, taste perversion, diarrhea, and epigastric discomfort). Also, most North American physicians should think twice before attempting to identify or treat H. pylori except in ulcer patients and other even smaller groups that can reasonably be anticipated to profit from eradication. Treating non-ulcer dyspeptic patients for H. pylori is usually quite disappointing in North America where symptoms frequently persist despite effective eradication.

Pharmacology Update

Rotigotine Transdermal System (Neupro®)

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

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

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

THE FDA HAS APPROVED A TRANSDERMAL PATCH FOR the treatment of early Parkinson's disease. Rotigotine is a non-ergoline, D3/D2/D1 dopamine receptor agonist. It is marketed by Schwarz Bioscience as Neupro.

Indications

Rotigotine is indicated for the treatment of the signs and symptoms of early stage idiopathic Parkinson's disease.[1]

Dosage

The recommended initial dose is 2 mg/24 hours. It may be titrated by 2 mg/24 hours weekly to maximum dose of 6 mg/24 hours. No dosage adjustment is required for moderate hepatic dysfunction or mild to severe renal dysfunction. The patch should be applied to clean, dry, healthy skin on the stomach, thigh, hip, flank, shoulder or upper arm.[1]

Rotigotine transdermal system is available as 2 mg/24 hours, 4 mg/24 hours and 6 mg/24 hours.

Potential Advantages

Rotigoline provides a once daily application that delivers a constant level of drug over 24 hours without regard to meals. In comparison, oral formulations tend to have inconsistent absorption, which may lead to variable pharmacological effects.[2] Rotigoline has low potential for drug-drug interactions involving CYP isoenzymes.[3]

Potential Disadvantages

Some patients may experience sudden excessive drowsiness without warning that may occur one year after initiation of treatment. The transdermal formulation contains sodium metabisulfite that may cause an allergic reaction (anaphylactic type) in certain susceptible individuals. The most common adverse event is application site reactions (37% vs 14% for placebo) and nausea (38% vs 15%). Other adverse events include syncope, weight gain, peripheral edema, and hypotension.[1]

Comments

Rotigotine is a potent nonergoline dopamine agonist similar to ropinirole and pramipexole. The efficacy of rotigoline was demonstrated in 3 randomized, double-blind placebo controlled parallel studies in patients with early Parkinson's disease, not currently taking levodopa or a dopamine agonist. The primary outcome was change from baseline for Part II (activity of daily living) and III (motor component) of the Unified Parkinson's Disease Rating Scale (UPDRS). Doses of 6 to 8 mg/24 hours showed a difference from placebo in the combined Parts II and III of -4.5 to -5.3 over a period of 11 to 37 weeks.[1,4] Baseline UPDRS ranged from 27.1 to 33.2. The reduction in score represents a 14% to 18% change. In patients with advanced disease, rotigoline added to levodopa decreased mean "off" time by an additional 1.8 hours (8 mg/24 hours) from a baseline 6.7 hours compared to placebo.[5] Fifty seven percent of patients showed a 30% or greater reduction in "off" time compared to 34% for placebo. Common adverse events

include application site reactions, nausea, vomiting, and somnolence. Serious adverse events include falling asleep during daily activity. Comparative studies with other dopamine agonists, levodopa, or MAO inhibitors (selegiline) have not been published. The product information indicated that one arm of a foreign study included an active oral comparator but it was not identified. The cost of rotigoline transdermal systems was not available at the time of this review.

Clinical Implications

Rotigotine transdermal is a new delivery system for an antiparkinson drug. It appears to offer some potential advantages over oral formulations such as more consistent delivery of the drug. Pulsatile stimulation of the striatal dopamine receptors resulting from short acting dopaminergic drugs may contribute to motor complications of Parkinson's disease.[6] Long-acting dopamine agonists such as cabergoline have been shown to reduce the frequency and delay the occurrence of motor complications.[7] Whether rotigotine offers a clear clinical advantage over existing agents remains to be established. ■

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CME Questions

29. Compared with a low fat diet, a low-glycemic diet is more likely to:
a. contain potatoes
b. stimulate appetite in those who have high insulin levels after glucose challenge.
c. elevate the high-density lipoprotein (HDL) level
d. exacerbate a pre-existing metabolic syndrome

30. Which of the following groups in the United States have been found to have an increased incidence of benign leukopenia without any increased risk for infection?
a. Mexican-Americans
b. African-Americans
c. smokers
d. all of the above
e. none of the above

31. The two five-day sequential regimens for the eradication of H. pylori provided what level of eradication compared to the 77% accomplished with standard 10-day triple therapy.
a. 80%
b. almost identical results
c. 53%
d. 89%
e. 95%

Answers: 29(c); 30(b); 31(d)

CME Objectives

The objectives of *Internal Medicine Alert* are:
- to describe new findings in differential diagnosis and treatment of various diseases;
- to describe controversies, advantages, and disadvantages of those advances;
- to describe cost-effective treatment regimens;
- to describe the pros and cons of new screening procedures.

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

Dr. Kuritzky is a consultant for GlaxoSmithKline and is on the speaker's bureau of GlaxoSmithKline, 3M, Wyeth-Ayerst, Pfizer, Novartis, Bristol-Myers Squibb, AstraZeneca, Jones Pharma, and Boehringer Ingelheim.

Dietary Intervention for Fatty Liver Disease: Fat or Carbohydrate Restriction?

The spectrum of nonalcoholic fatty liver disease (NAFLD) can range from asymptomatic accumulation of fat in the liver without inflammation, to non-alcoholic Steatohepatitis (NASH). Because NASH is an inflammatory condition, it ultimately leads to fibrosis and even end-stage liver disease in some. Increasing numbers of obese and diabetic individuals result in clinicians encountering NAFLD regularly.

Initial treatment recommended for NASH is weight loss. Major consensus groups (eg, American Heart Association, American Diabetes Association) have advocated a diet with less than 30% fat. Typically, however, fat restriction is compensated by an increase in dietary carbohydrate, which can induce deleterious metabolic consequences to insulin levels and triglycerides.

To study the impact of fat vs carbohydrate restriction, 52 obese individuals were given a calorie-restricted diet containing 15% protein. The remainder of calories was then divided as either 60% carbohydrate/25% fat or 40% carbohydrate/45% fat.

The amount of weight loss was equal in the two groups over 16 weeks. Serum alanine aminotransferase levels decreased significantly more in the group assigned to low carbohydrate, suggesting reduced fat-induced hepatic inflammation. The authors suggest that a carbohydrate restricted, moderately fat enhanced diet provides physiologic benefits for obese individuals compared to dietary advice currently recommended. ■

Ryan MC, et al. Diabetes Care. 2007;30(5):1075-1080.

Motivational Interviewing to Enhance Weight Control in Diabetic Women

Motivational Interviewing (M-INT) is not a generic term, but rather a specific process of techniques that have proven successful in diverse health issues; fundamentally, it is based upon an exploration of a person's rationale for change, coupled with elucidation of their own ambivalence, looking into discrepancies between current behavior and core values/personal goals.

Overweight diabetic women (n = 217) were enrolled in an 18 month randomized controlled trial. All subjects participated in an intensive behavioral weight control program with guidance by a multidisciplinary team including psychologists, dietitians, exercise counselors, and diabetes educators to assist with caloric restriction (1200-1500 kcal/day). Half the group also received M-INT, administered as five individual sessions (45 minutes) at baseline, 3, 6, 9, and 12 months.

Both groups experienced weight loss, but the M-INT group lost more weight at each measurement point (eg, 4.8 kg vs 2.7 kg at 12 months). Although the A1c improvement seen in the M-INT group was superior at six months, by eighteen months, the groups were similar. The results of this data should have wide generalizability, because the study subjects were ethnically diverse (eg, 38% African American). Whether male subjects would enjoy similar benefits has not yet been studied. ■

West DS, et al. Diabetes Care. 2007;30(5):1081-1087.

One-stop Shopping for Osteoporosis Treatment

Management of osteoporosis (OSPS) has evolved from daily treatment with bisphosphonates, to weekly or even monthly administration. There is some support for the concept that every step towards dosing parsimony improves likelihood of compliance, keeping in mind, however, that with treatment regimens employing infrequent dosing, each omissive error is also more consequential!

Zoledronic acid (ZDA) is a parenteral bisphosphonate (BIS), and is felt to work by similar mechanism to oral BIS (ie, alendronate, ibandronate, risedronate). The notoriously poor bioavailability of oral BIS requires strict administration techniques, without which absorption is severely compromised. As many as 50% of persons prescribed oral BIS have been documented to be nonadherent after a single year of use.

A double-blind placebo-controlled trial of ZDA in postmenopausal women with OSPS (n = 7,765) monitored new vertebral fractures and hip fractures over 36 months. ZDA was administered as a one-time 15-minute intravenous infusion of 5 mg each year for 3 years.

Over 3 years, ZDA reduced vertebral fractures by 70%, and hip fracture by 41%. Bone mineral density was improved. Markers of bone turnover were improved. The results attained equal or surpass those shown in clinical trials of oral BIS. One case of osteonecrosis was seen in the treatment group, but one was also seen in the placebo group. Although atrial fibrillation was seen more often in the ZDA group (mechanism unknown), adverse events associated with atrial fibrillation such as stroke were similar in both groups. ■

Black DM, et al. N Engl J Med. 2007;356:1809-1822.

Why Does the QRS Widen?

By Ken Grauer, MD, *Professor, Department of Community Health and Family Medicine, University of Florida*
Dr. Grauer is the sole proprietor of KG-EKG Press, and publisher of an ECG pocket brain book, and reports no financial relationship to this field of study.

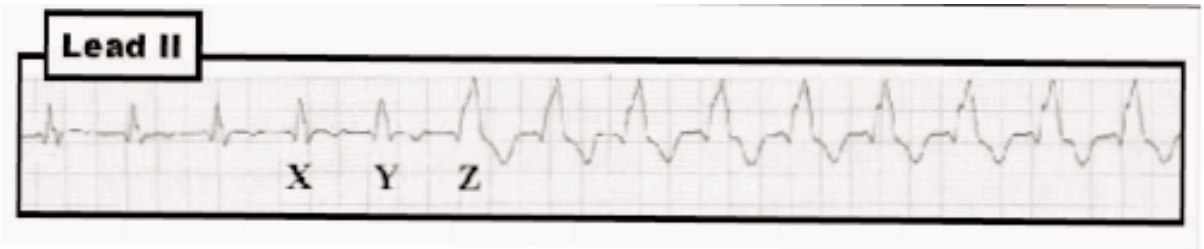

Figure. Lead II rhythm strip obtained during cardiac arrest.

Clinical Scenario: The lead II rhythm strip shown below was obtained from a middle-aged man in cardiac arrest. The patient had multiple co-morbidities, including end-stage renal disease (on dialysis), a history of cocaine abuse, and severe, non-ischemic cardiomyopathy. No pulse could be felt at the time this tracing was recorded. What is the rhythm? Why does the QRS complex widen (from beat Z onward)? What are the clinical implications of this rhythm in the setting of cardiac arrest?

Interpretation/Answer: The rhythm is regular at a rate of 110/minute. Looking first at the initial part of the tracing, the QRS complex appears to be of borderline duration (about half of a large box, or 0.10 second). No atrial activity is seen in this lead II monitoring lead. Although it would be helpful to see other leads (ideally a 12-lead tracing) to better ascertain QRS duration and the presence or absence of atrial activity, the lack of a clear upright P wave in lead II strongly suggests that this is not a sinus rhythm. Our best guess from this single lead tracing is that the rhythm represents a junctional (AV nodal) tachycardia at 110/minute. The QRS complex actually begins to widen (ever so slightly) with beat Y. It then dramatically widens from beat Z onward. This is not the onset of a new ventricular rhythm! We say this because there is absolutely no change in the rate over the entire tracing. Similarly, there is no introduction of atrial activity. We therefore surmise that this is a junctional tachycardia at a constant rate with development over several beats of a conduction (bundle branch block) delay that occurred during this patient's cardiac arrest. Among the reasons why this may occur in this setting is hypoxemia from lack of coronary perfusion.

The rhythm in this case therefore is PEA (pulseless electrical activity), which by definition entails the presence of an electrical rhythm in the absence of a palpable pulse. In recent years, PEA has become the most common mechanism of cardiac arrest (surpassing ventricular fibrillation). It is generally the end–result of some underlying process. Overall prognosis is unfortunately poor, especially when the underlying cause of the PEA is not reversible.

This patient expired despite resuscitative attempts. ■

In Future Issues: **Is The Hope of Virtual Colonoscopy Being Vaporized?**

PHARMACOLOGY WATCH

Supplement to Clinical Cardiology Alert, Clinical Oncology Alert, Critical Care Alert, Infectious Disease Alert, Internal Medicine Alert, Neurology Alert, OB/GYN Clinical Alert, Primary Care Reports, Travel Medicine Advisor.

Risk With Preventative Antibiotics Outweighs Benefit for Most

Sweeping new changes have been made to the guidelines for prevention of endocarditis in patients undergoing dental procedures. The new recommendations dramatically reduce the indications for dental prophylaxis and reduce the number of patients who need preprocedure antibiotics. The guideline was issued by the American Heart Association in conjunction with the American Dental Association, Infectious Diseases Society of America, and the Pediatric Infectious Diseases Society and was published online April 19, 2007, in *Circulation*. The guidelines reflect evidence that the risk of taking preventative antibiotics outweighs the benefit for most patients. It is also been found that infectious endocarditis (IE) is more likely to result from frequent exposure to random bacteremias from activity such as flossing and brushing than from dental work. Specifically, the guidelines say that prophylactic antibiotics are no longer required for patients with mitral valve prolapse, rheumatic heart disease, bicuspid valve disease, calcified aortic stenosis, or congenital heart conditions such as ventricular septal defect, atrial septal defect, and hypertrophic cardiomyopathy. There are still patients who are at extremely high risk of IE who should continue to receive prophylactic antibiotics: patients with artificial heart valves, a history of infective endocarditis, congenital heart disease including unrepaired or incompletely repaired cyanotic congenital heart disease, including those with palliative shunts and conduits, those with a completely repaired congenital heart defect with prosthetic material during the first 6 months after the procedure, repaired congenital heart defect with residual defect at the site or adjacent to the site of a prosthetic patch or prosthetic device, or a cardiac transplant patient with a cardiac valvulopathy. Antibiotic prophylaxis is no longer recommended for any other form of congenital heart disease. Dosing regimens are essentially the same as previous recommendations and include oral amoxicillin 2 gm 30 to 60 minutes prior to procedure. Oral alternatives include cephalexin, clindamycin, azithromycin or clarithromycin. Parenteral regimens include ampicillin, cefazolin, ceftriaxone, and clindamycin. The guideline also no longer recommends antibiotics to prevent IE in patients undergoing genitourinary or gastrointestinal tract procedures (*Circulation* 2007, doi:10.1161/CIRCULATIONAHA.106.183095). The full guideline is available at http://www.ada.org/prof/resources/ topics/infective_endocarditis_guidelines.pdf. ■

Gonococcal Infections, CDC's Updated Treatment

The CDC has issued updated treatment recommendations for gonococcal infections and associated conditions due to the high level of resistance of gonorrhea to fluoroquinolones. The agencies Gonococcal Isolate Surveillance Project demonstrates that fluoroquinolone-resistant gonorrhea is continuing to spread and is now widespread

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throughout United States. Therefore, fluoroquinolones such as ciprofloxacin, ofloxacin, or levofloxacin are no longer recommended. Current recommended regimens for gonococcal infections of the cervix, urethra, and rectum are ceftriaxone 125 mg IM and a single dose or cefixime 400 mg orally in a single dose plus treatment for chlamydia if chlamydial infection is not ruled out. Uncomplicated gonococcal infections of the pharynx should be treated with ceftriaxone 125 mg IM plus treatment for chlamydia, if chlamydial infection is not ruled out. Disseminated gonococcal infection should be treated with ceftriaxone 1 g IM or IV every 24 hours. Pelvic inflammatory disease may be treated with parenteral and oral therapy. Parenteral therapy regimens include cefotetan or cefoxitin plus doxycycline or clindamycin plus gentamicin. An alternative regimen is ampicillin/sulbactam plus oral doxycycline. Oral therapy can be considered in women with mild to moderate disease. With the loss of fluoroquinolones, cephalosporins are the mainstay of most regimens. For patients who are highly allergic to cephalosporins, spectinomycin may be considered although it is not generally available in this country. Another option is azithromycin, however, prescribing should be done in consultation with an infectious disease specialist due to concerns over emerging antimicrobial resistance to macrolides. The CDC's full recommendations are available online at www.cdc.gov/std/treatment/2006/updated-regimens.htm. ■

Head Lice — Malathion First-Line Treatment

Malathion should be first-line treatment for children who have lice according to a new review in the journal *Pediatrics*. Head lice have become resistant to nearly all first-line treatments in United States including permethrin, which has been considered first-line treatment for years. Malathion, in the formulation containing isopropyl alcohol and terpineol, is safe and effective for lice and all existing points within the life cycle, and generally requires a single treatment, reducing the duration of infestation, and lost time from school and work. Concern about flammability seems to be over emphasized, as there have been no reported cases of bodily injury related to burns (*Pediatrics* 2007. 119:965-974).

Statins, May Cut the Risk of Cataracts

Statins, the cholesterol wonder drugs, have been associated with a number of other benefits including reduction of inflammation within the arteries, improved bone density, reduction in the risk of colon cancer, renoprotective effects, and reduction in the risk of Alzheimer's disease and other dementias. Now, a new study suggests that the drugs may also cut the risk of cataracts by 50%. Researchers from Australia reviewed the rate of cataract development in 3,654 elderly patients. After 10 years, after controlling for age, gender and others factors, the hazard ratio for any type of cataract in statin users was 0.52. In subgroups, there was a decreased risk of nuclear cataracts (HR = 0.66) and cortical cataracts (HR =0.76), but neither of these reached statistical significance. The authors conclude that there may be a protective influence of statins on cataracts and this needs to be further explored (*Am J Ophthalmol* 2007; 143:687-689). ■

FDA Actions

Sanofi Aventis has been approved to produce a vaccine to prevent bird flu in humans. The vaccine against the H5N1 virus will not be produced commercially, but will instead be stockpiled by the U.S. government for distribution in case of the outbreak. The FDA admits that the vaccine is not optimal, requiring a higher dose than normal flu vaccine, and 2 shots which must be given 28 days apart. But until other vaccines are developed, this vaccine will be used as the "interim measure."

The FDA is recommending updating black box warning regarding suicidality in young adults (under age 24) starting on antidepressants, calling for appropriate monitoring and close observation. The new recommendation should also include the statement that there was no increase in suicidality in adults over the age of 24, and a decrease in the risk in adults over the age of 64.

The FDA has approved generic versions of 2 of the most popular drugs of the last decade, Ambien (zolpidem) and Zoloft (sertraline). Zolpidem will be available in 5 mg and 10 mg immediate-release tablets. Thirteen manufactures have received approval to market the product. Sertraline is approved in the 25 mg, 50 mg and 100 mg strengths, and will be produced by Ranbaxy Laboratories.

The FDA has issued a warning about the health risks of dietary supplements touted as sexual enhancement products and treatments for erectile dysfunction that have been distributed under the trade names True Man and Energy Max. Both drugs have been sold throughout United States. Energy Max was found to contain an analogue of sildenafil, the active ingredient in Viagra, while True Man was found to contain an analogue of sildenafil and vardenafil, the active ingredient in Levitra. Both drugs can have serious interactions with nitrates. ■