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Internal Medicine

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ABSTRACT & COMMENTARY

Can Answering a Phone Call Give You Cancer?

By Seema Gupta, MD, MSPH

Primary Care Physician, Charleston, WV

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

SYNOPSIS: In a pooled analysis of two case-control studies, mobile and cordless phone use increased the risk of glioma and that risk increased significantly with years and hours of use.

SOURCE: Hardell L, et al. Mobile phone and cordless phone use and the risk for glioma — Analysis of pooled case-control studies in Sweden, 1997-2003 and 2007-2009. *Pathophysiology* 2014 Oct 29. pii: S0928-4680(14)00064-9. doi: 10.1016/j.pathophys.2014.10.001. [Epub ahead of print].

In the past decade, cellular phone usage has grown exponentially worldwide, and this use is prevalent in all age groups, including children. Currently, more than 90% of the populations in the United States and Western Europe utilize this mode of wireless communication. This has raised concerns for health risks due to a greater exposure to radiofrequency electromagnetic fields. These radiations are considered non-ionizing, meaning that they do not have sufficient energy to break off electrons from their orbits around atoms and ionize the atoms, such as ionizing radiations. Previous studies have suggested that these radiofrequency signals emanating from cellular phones, cordless phones, and other devices may have biologic effects on target cells or tissues.[1,2] Brain tissue is the main target of such radiation exposure, especially on the side of the brain where the mobile device is regularly used. The brain tumors associated with the use of cellular phones are the malignant types, mostly glioma, and a benign tumor, acoustic neuroma.[3] In contrast, no consistent pattern of an association has been found for the most common benign brain tumor, meningioma. With the average age to begin cell phone use declining in the recent years, children may be at particular risk owing to the duration of exposure to radiations as well as the potential to absorb at higher rates due to high conductivity as a result of smaller head size and thinner

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skull bones. Long-term use data provide an opportunity to conduct more detailed analysis on the relationship between such radiation exposure and the risk for the development of brain tumors.

In their study, Hardell et al conducted a pooled analysis of two Swedish case-control studies on malignant brain tumors with patients diagnosed during 1997–2003 and 2007-2009 from six administrative regions with oncology centers covering newly registered cancer cases in Sweden. The trial included both men and women ages 20-80 years (1997-2003) and 18-75 years (2007-2009) at the time of diagnosis. Only cases with histopathological verification of the tumor were included. Exposure was assessed using a mailed questionnaire for each participant. Overall, 1498 (89%) cases and 3530 (87%) controls participated in the study.

Researchers found that an increased risk for glioma was associated with use of both cellular and cordless phones, and that risk increased significantly with years and hours of use. Study participants who talked on cellular phones for more than 25 years had a statistically significant three-fold increased risk (odds ratio [OR] = 3.0; 95% confidence interval [CI] = 1.7–5.2) compared to those who used wireless phones for less than a year. Overall, the use of cellular phone increased the risk of glioma (OR = 1.3; 95% CI = 1.1-1.6). Similarly, in cordless phone users, there was an increase in risk (OR = 1.4; 95% CI = 1.1-1.7), with the highest risk in the > 15–20 years latency group (OR = 1.7; 95% CI = 1.1–2.5). The odds ratio increase was found to be statistically significant for both per 100 hours of cumulative use and per year of latency for cellular and cordless phone use. The researchers found the highest odds ratio for ipsilateral cellular or cordless phone use (OR = 1.8; 95% CI = 1.4-2.2 and OR = 1.7; 95% CI = 1.3-2.1, respectively). Most of the types of malignant brain tumors were glioma (n = 1380; 92.1%) with the most malignant variety, astrocytoma grade IV (glioblastoma multiforme) comprising 50.3% of such gliomas.

■ COMMENTARY

The authors have found additional evidence suggesting a possible association between brain tumors and wireless phone devices. This could be possibly explained by the electromagnetic fields disrupting the ability of brain cells to repair the damaged DNA or potentially causing gene mutations. However, we should be careful in noting that an association does not automatically equate to causation. The carcinogenic effect of radiofrequency electromagnetic field on humans was evaluated by a panel of scientists at the World Health Organization's (WHO) International Agency for Research on Cancer in 2011.[4] The Working Group categorized these non-ionizing radiations being emitted from mobile phones and other devices as a Group 2B (i.e., a "possible carcinogen" in humans). However, it is significant to note that not all studies thus far have demonstrated a consistent link between cell phone use and cancers of the brain. The INTERPHONE study group found that there was no increase in risk of acoustic neuroma with the regular use of a mobile phone or for users who began regular use 10 years or more before the reference date.[5] The National Cancer Institute's position is that there has not been a consistent link demonstrated between cell phone use and cancers of the brain, nerves, or other tissues of the head or neck. It is clear that further research is needed to establish whether there is a cause and effect relationship between radiations emitted by wireless devices and brain tumors. The best advice to our patients presently may be to disclose that such radiations are considered a possible carcinogen by the WHO and further research is ongoing. However, for children, it may be pertinent to recommend avoiding excess contact with such devices such as sleeping with their cellular phone under the pillow. ■

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ABSTRACT & COMMENTARY

Liraglutide Preserves Beta Cell Function — Well, Kind of…

By Jeff Unger, MD

Director, Unger Primary Care Concierge Medical Group, Rancho Cucamonga, CA

Dr. Unger serves as an advisor, speaker and clinical investigator for Novo Nordisk.

SYNOPSIS: Fifty-one patients with type 2 diabetes of 2.6 +/- 1.9 years duration and an A1C of 6.8 % completed 4 weeks of intensive insulin therapy in order to eliminate glucose toxicity which is injurious to pancreatic beta cells. Thereafter, patients were randomized to receive daily subcutaneous liraglutide or an equivalent volume of placebo. Serial assessments of beta-cell function following oral glucose tolerance testing was performed at 12 week intervals for 48 weeks. Patients using liraglutide noted a rebust enhancement of beta cell function which was sustained over the course of the trial, yet lost within two weeks after stopping treatment.

SOURCE: Retnakaran R, et al. Liraglutide and the preservation of pancreatic beta-cell function in early type 2 diabetes. The LIBRA Trial. *Diabetes Care* 2014;37:3270-3278.

Type 2 diabetes is characterized by progressive loss of beta cell function over time. Beta cell loss occurs via two mechanism; a) glucotoxicity (i.e., chronic elevation of plasma glucose levels > 240 mg/dL) and b) programmed cell death (apoptosis — which is genetically determined and triggered by multiple environmental factors). Short-term intensive insulin therapy provided to patients with type 2 diabetes eliminates glucotoxicity creating a level playing field upon which to objectively evaluate the potential beta-cell protective potential of anti-diabetic medications.

Liraglutide is a GLP-1 receptor agonist with multiple beneficial metabolic effects, including glucose-dependent stimulation of insulin secretion from pancreatic beta-cells, suppression of postprandial glucagon secretion, slowing of gastric emptying, enhanced glucose disposal within myocytes, weight-loss promotion, and preclinical data favoring beta-cell mass augmentation in animal models. The objective of the Liraglutide and Beta-Cell Repair (LIBRA) trial was to evaluate the effect of liraglutide on the preservation of beta-cell function over 1 year in patients with early type 2 diabetes following the amelioration of glucose toxicity with intensive insulin therapy.[1-3]

The primary outcome of baseline-adjusted insulin secretion-sensitivity index-2 (a measure of beta-cell function) at 48 weeks was 339.8 +/- 27.8 vs 229.3 +/- 28.4 for the liraglutide vs. placebo cohort (P = 0.008). The baseline-adjusted A1C was 6.2% vs. 6.6% for the liraglutide vs. placebo group (P = 0.055). No difference was noted in the incidence of hypoglycemia among the two groups. Two weeks after stopping treatment, the beneficial effect of ISSI-2 of liraglutide vs placebo was entirely lost (191.9 +/- 24.7 vs. 238.1 +/- 25.2; P = .20).

■ COMMENTARY

Early initiation and maintenance of liraglutide certainly suggests that beta-cell preservation is possible. Liraglutide offers many advantages as an antidiabetic agent. Liraglutide can effectively reverse seven of the eight pathogenetic defects that result in hyperglycemia. The addition of an SGLT-2 inhibitor to liraglutide will effectively reverse all eight of DeFronzo's ominous octet. The drug is simple to use, lowers fasting and postprandial hyperglycemia, and minimizes one's risk of hypoglycemia. The drug can be used in patients with chronic kidney disease as well as those taking basal insulin. Patients should be admonished to remain adherent to their liraglutide prescriptions, as premature termination of the drug can result in loss of beta-cell function and glucose toxicity. ■

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ABSTRACT & COMMENTARY

Paradoxical Low-flow, Low-gradient AS

By Michael H. Crawford, MD

SYNOPSIS: The authors concluded that a majority of patients with PLF-LG AS have severe stenosis as defined by valve weight after surgery, and the valve gradient may underestimate stenosis severity in such patients.

SOURCE: Clavel MA, et al. Paradoxical low-flow, low-gradient aortic stenosis despite preserved left ventricular ejection fraction: New insights from weights of operatively excised aortic valves. *Eur Heart J* 2014;35:2655-2662.

Low-flow, low-gradient aortic stenosis (AS) is usually associated with reduced left ventricular (LV) performance. When LV systolic function is normal, it has been labelled "paradoxical." Such patients have considerable concentric LV hypertrophy and a restrictive physiology with a normal LV ejection fraction (EF) but low stroke volume. The prognosis of these patients compared to those with similar severity of AS but normal stroke volume is unclear from the literature, raising the questions of whether AS severity can be determined accurately. Thus, these investigators from Quebec, Canada, hypothesized that aortic valve weight after excision at surgery would be a surrogate for AS severity, and sought to compare it in the paradoxical low-flow, low-gradient (PLF-LG) patients vs AS patients with normal flow and high gradients (NF-HG). They studied two groups: 250 patients with severe AS (valve area ≤ 1.0 cm^2 and index ≤ 0.6, n = 33) and either paradoxical AS or high-flow, high-gradient AS (n = 105) undergoing surgical aortic valve (AV) replacement, and 150 patients with moderate-to-severe AS with NF-HG undergoing AV replacement during coronary bypass surgery. The latter group was used to define a valve weight cutoff for severe AS using echo Doppler as the standard.

Baseline data showed that PLF-LG patients had more dyslipidemia and coronary artery disease. PLF-LG patients had smaller LVs with lower mass than NF-HG patients. Interestingly, BNP levels and AV area were not different between these two AS groups. There were more patients with bicuspid valves in the NF-HG group (42% vs 15%, P = 0.003). AV weight was higher in the NF-HG group compared to the PLF-LG group (P = 0.02), but when dichotomized by sex, the difference was not significant in women. Using the established AV weigh cutoff from the 150 patients with moderate-to-severe AS undergoing coronary artery bypass grafting (CABG) plus AV replacement, severe AS was present in 70% of the PLF-LG group and 86% of the NF-HG patients. This finding was also only significant in men. The authors concluded that a majority of patients with PLF-LG AS have severe stenosis as defined by valve weight after surgery, and the valve gradient may underestimate stenosis severity in such patients.

■ COMMENTARY

This is a novel approach to studying patients with low-flow, low-gradient AS. A major issue in studying these patients is determining the gold standard for measuring AS severity. Many studies in the area suffer from measurement errors, failure to take body size into consideration, and lack of a more in-depth analysis of orifice area. They chose the weight of the aortic valve excised at surgery as compared to a comprehensive Doppler-echo evaluation to establish a weight cutoff for severe AS in patients with moderate-to-severe AS undergoing CABG and AV replacement. They then applied this cutoff to selected patients presumed to have severe AS who had an isolated AV replacement by surgery. The patients selected were divided into two groups: NF-HG and PLF-LG, the latter being paradoxical because their left ventricular ejection fraction (LVEF) was normal. More than 80% of the NF-HG patients of either sex had severe AS by valve weight and 65-80% of PLF-LG patients, depending on sex, had severe AS. These finding validate their selection criteria for surgery, but, more importantly, highlight the fact that patients with normal LVEFs with low-flow, low-gradient AS on echo often have severe AS and benefit from valve replacement.

How do we identify the PLF-LG patients who have severe AS? The authors suggest a multimodality approach. Clinically, these patients often have considerable hypertrophy with small cavity sizes, normal LVEF, but reduced longitudinal function and high valve-arterial impedance. The first step is a comprehensive echo-Doppler approach to quantifying AV area, which could include dobutamine stress testing to identify pseudo AS and transesophageal echo to measure orifice area. If there is still uncertainty, a CT scan to quantify AV calcium content could be helpful. In this study, brain natriuretic peptide was not particularly useful. Also, in this study, only echo-Doppler AV area at rest was used to clinically characterize the patients and make surgical decisions. So this multimodality approach has not been prospectively tested. ■

PHARMACOLOGY UPDATE

Human Papillomavirus 9-valent Vaccine, Recombinant (Gardasil®9)

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

The FDA has approved a 9-valent human papillomavirus (HPV) vaccine. The new vaccine covers five more types of HPV than the previous vaccine and protects against 90% of the HPV strains that cause cervical cancer.[1] The new vaccine is marketed by Merck as Gardasil®9.

INDICATIONS

HPV-9 vaccine is indicated in girls and women ages 9 through 26 years of age for the prevention of cervical, vulvar, vaginal, and anal cancer caused by HPV types 16, 18, 31, 33, 45, 52, and 58; and genital warts by HPV types 6 and 11.[2] It is also indicated for the prevention of precancerous or dysplastic lesions (cervical, vulvar, anal, and vaginal intraepithelial neoplasia (CIN, VIN, AIN, VaIN) and cervical adenocarcinoma (AIS). HPV-9 is also indicated in boys ages 9-15 years to prevent anal cancer, genital warts, and precancerous or dysplastic lesions (anal intraepithelial neoplasia).

DOSAGE

The recommended dose is one injection (0.5 mL) intramuscularly, with follow-up injections at 2 and 6 months. HPV-9 can be given concomitantly with meningococcal vaccine (Menactra) and Tdap (Adacel). HPV-9 is supplied as a single-dose vial or prefilled syringe.

POTENTIAL ADVANTAGES

The relative contributions increase the overall coverage for cervical cancer-causing strains to 90% wordwide and to 95% in North America.[1]

POTENTIAL DISADVANTAGES

The duration of immunity has not been established.[2] The most frequent adverse events are injection site pain (72-90%), injection site swelling (27-49%), and injection site erythema (25-42%).[2] Injection site reactions appear to be more frequent in girls and women than boys. Injection site reactions were numerically higher for HPV-9 vs. HPV-4. Syncope may occur, so observation for 15 minutes after administration is recommended.

COMMENTS

The clinical studies with HPV-9 were based on the efficacy of HPV-4.[2] In a large study in girls and women ages 16-26 years (n = 14,204) who were naïve to the relevant HPV types, HPV-9 was compared to HPV-4. The primary endpoint was efficacy for the five additional HPV types (31, 33, 45, 52, and 58) at the 7-month visit. HPV-9 showed > 90% efficacy against cervical, vaginal, and vulvar cancers, cervical intraepithelial neoplasia, HPV-related vulvar or vaginal disease, HPV-related persistent infection, abnormal Pap test, HPV-related biopsy, and 88% protection against definitive therapy (loop electrosurgical excision procedure and conization) related to the five HPV types. Effectiveness against the four previous HPV types were considered noninferior based on comparable geometric mean titers (GMTs) between HPV-9 and HPV-4. The effectiveness in girls and boys ages 9-15 years were inferred from GMTs.[2] For all nine HPV types, the GMTs were 2-3-fold higher for the younger population relative to girls/women ages 16-26 years.[2] In subjects previously vaccinated with HPV-4, seropositivity was 98% or higher with HPV-9. Anti-HPV titers for types 31,33, 45, 52, and 58 were 25-63% of the titer seen in previously unvaccinated subjects.[2] The clinical relevance of this observation is not known.

CLINICAL IMPLICATIONS

HPV-9 vaccine provides additional coverage for about 20% of cervical cancers and 25%-30% of cervical precancers (CIN1, and CIN2/3) compared to the previous HPV vaccine.[3] The recommendation for use of HPV-9 will be considered at the Center for Disease Control and Prevention's Advisory Committee on Immunization Practice meeting in February 2015.[4] The wholesale cost is $489 for three doses. ■

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Clinical Briefs

By Louis Kuritzky, MD

Screening for Lung Cancer with Low-dose CT

SOURCE: Gould MK, et al. *N Engl J Med* 2014; 371:1813-1820.

The United States Preventive Services Task Force (USPSTF) gave a level B recommendation in support of annual low-dose computed tomography (LDCT) to screen for lung cancer in appropriate risk groups. The USPSTF decision was largely based on the National Lung Screening Trial (NLST), a mega-trial (n = 53,454) in the United States that randomized subjects to annual LDCT or chest X-ray. The primary endpoint of the study was lung cancer mortality, and all-cause mortality was a secondary endpoint. Inclusion criteria included at least a 30-pack/year history of smoking (if stopped within 15 years), ability and willingness to complete follow-up for abnormal findings, and absence of problematic comorbidities that might otherwise compromise long-term survival.

The good news is that LDCT was associated with a 20% relative risk reduction in lung cancer mortality and a 7% reduction in all-cause mortality, both of which were statistically significant. Should we end the discussion there?

Perhaps not. The NLST has several stark limitations. First, literally 95% of "positive" findings on LDCT were false-positive, and harms to patients during the follow-up evaluations were substantial, including deaths. Second, a not-inconsiderable number of "incidentalomas" were also detected, and follow-up data on whether these findings favorably (or unfavorably) affected study subjects' lives has not yet been published.

Finally, an issue about the absolute magnitude of benefit. Although the 20% relative reduction in lung cancer mortality sounds impressive, the absolute risk reduction was very small; In the LDCT group, 356 of 26,309 died (1.3%) vs 443 of 26,035 in the chest X-ray group (1.7%), for an absolute risk reduction of 0.348%.

Although most major organizations have endorsed USPSTF recommendations, the American Academy of Family Physicians (AAFP) has issued a note of caution, based on lack of replication of these data in a community setting. Instead of universal screening, AAFP suggest a "shared decision-making" approach reminiscent of its advice about prostate cancer screening in the recent past. ■

Rethinking Acetaminophen for Acute Low Back Pain

SOURCE; Williams CM. *Lancet* 2014;384: 1586-1596.

The natural history of acute low back pain indicates that somewhere between 60-70% of episodes have spontaneously resolved by 3 weeks and 80-90% by 3 months. We would hope that the goals of clinicians in their choice of pharmacotherapy and activities (physical therapy, exercise) are to shorten time to recovery, improve functional status during recovery, and provide symptom relief. A Cochrane Database analysis has confirmed the efficacy of NSAIDs for acute low back pain. What about acetaminophen? (Note: for readers who choose to review the original reference on this article, the word "paracetamol" is used in the original title, because that is the preferred term in the United Kingdom and Australia for what we call "acetaminophen" in the United States).

In this double-blind, placebo-controlled study conducted in Sydney, Australia, patients with acute low back pain (n = 1096) were randomized to treatment with PRN acetaminophen (up to 4000 mg/d) or placebo and followed for 3 months. The primary outcome was acute low back pain recovery, defined as a score of ≤ 1 on a 1-10 pain scale for at least 7 consecutive days.

No differences were found in time to recovery between groups. The authors suggest that although replication of their data with another clinical trial would make these conclusions more definitive, clinicians should be circumspect about use of acetaminophen in acute low back pain. ■

Non-obstructive Coronary Artery Disease: Not So Innocent After All

SOURCE: Maddox TM, et al. *JAMA* 2014;312: 1754-1763.

It has become abundantly clear that coronary events (i.e., myocardial infarction [MI]) are not simply a result of "clogged pipes." To the contrary, it has been documented that the majority of plaque ruptures occur within coronary arteries that have been atherosclerotically categorized as "non-obstructive." In this report, obstructive coronary disease was defined as ≥ 50% stenosis of the left main coronary artery or ≥ 70% stenosis in other coronary arteries. Non-obstructive coronary disease was defined as 20-49% stenosis, and < 20% stenosis was categorized as "no apparent (coronary artery disease) CAD."

The authors of this report studied all patients who underwent coronary arteriography in Veterans Adminstration hospitals from 2007-2012 (n = 37,684). Within this cohort, 8384 patients were reported to have non-obstructive coronary disease. They tracked the rate of admission for acute MI in the year following arteriography.

Compared to persons with no apparent CAD, the hazard ratio for MI at 1 year for persons with non-obstructive coronary disease was 2.0-4.5 (dependent upon the number of vessels involved); for persons with obstructive CAD, the hazard ratio was 9.0-19.5 (dependent on the number of vessels involved). ■

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CME QUESTIONS

1. **In the study by Hardell et al, mobile and cordless phone use was associated with a risk for:**
   a. Astrocytoma
   b. Gliomac.
   c. Lymphoma
   d. Meningioma

2. **Which of the following tests is used to evaluate beta cell function in the study by Retnakaran et al?**
   a. Fasting C-peptide
   b. A1C
   c. Insulin secretion-sensitivity index-2
   d. HOMA-B

3. **In patients with low-flow, low-gradient, but a normal LVEF, what percentage have severe AS by valve weight?**
   a. 25%
   b. 50%
   c. 70%
   d. 90%

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]

The Economic Burden of Undiagnosed Pre-diabetes … A Call For Action

Should Clinicians Discuss Resumption Of Sexual Activity Following An Acute Myocardial Infarction?

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.

Ongoing Chest Pain with Precordial Lead Findings

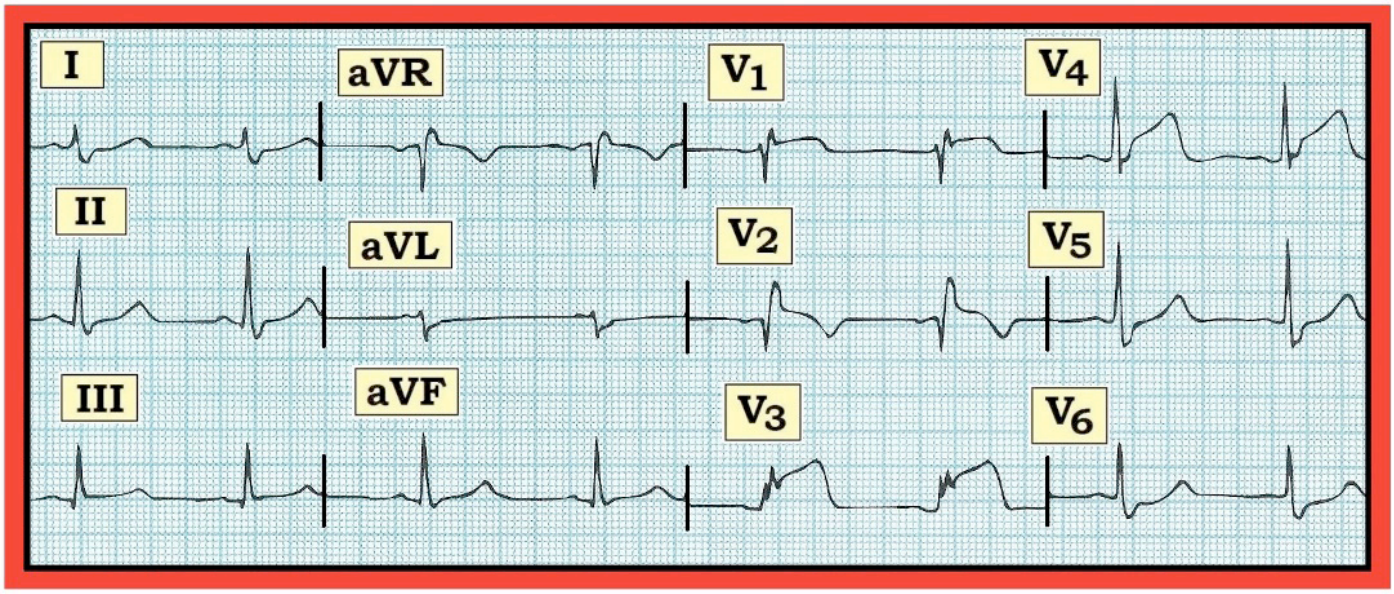

Figure: ECG from a patient with ongoing chest pain.

Interpretation: The rhythm is sinus at about 60/minute. The QRS complex appears to be slightly prolonged — at least in certain leads. This emphasizes the importance of assessing interval duration in all 12 leads, since the QRS complex does not appear widened in leads III, aVL, and aVF. An rSR' pattern is seen in lead V1, in association with wide terminal S waves in lateral leads I and V6. This is consistent with (right bundle branch block) RBBB — which we would classify as "complete" because: 1) The QRS complex is prolonged to at least 0.11 second; and 2) In addition to the rSR' in lead V1, there are wide terminal S waves present in both leads I and V6.

Two important differences between complete RBBB and complete (left bundle branch block) LBBB are that the QRS complex does not need to be as prolonged with RBBB (because the right ventricle is thinner than the left ventricle) and infarction Q waves may be seen much more easily with RBBB, because this conduction defect does not alter initial depolarization of the ventricular septum the way that LBBB does. Although a small initial positive deflection (r wave) is seen in lead V1 of this tracing, a wide and deep Q wave is seen in lead V2. This indicates anterior infarction has occurred.

- In addition to this Q wave in lead V2, there is prominent ST elevation in leads V1 through V4. This should not be seen with simple RBBB.
- A final subtle finding is slight-but-real ST segment depression in lead V6. ST depression is not seen in other leads.

In summary, the important findings on this ECG include: 1) sinus rhythm at a relatively slow rate of 60/minute; 2) complete RBBB; 3) marked anterior ST segment elevation in association with a Q wave in lead V2; and 4) subtle ST depression in lead V6, that may represent a "reciprocal" change. Despite the presence of RBBB, these findings indicate anterior infarction of uncertain age. Persistence of marked anteroseptal ST elevation in this patient with ongoing chest pain suggests anteroseptal infarction may still be in active evolution. ■

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• identify cost-effective treatment regimens; and
• explain the advantages and disadvantages of new disease screening procedures.

The American Medical Association, which oversees the Physician's Recognition Award and credit system and allows AHC Media to award AMA PRA Category 1 Credit™, has changed its requirements for awarding AMA PRA Category 1 Credit™. Enduring materials, like this newsletter, are now required to include an assessment of the learner's performance; the activity provider can award credit only if a minimum performance level is met.

Here are the steps for earning credit for this activity:
1. Read and study the activity, using the provided references for further research.
2. First-time users must register on the site using the 8-digit subscriber number printed on your mailing label, invoice or renewal notice. On and after Jan. 5, when logging onto the new AHCMedia.com, go to "MyAHC" and then "My Courses" to view your available continuing education activities.
3. Pass the online tests with a score of 100%; you will be allowed to answer the questions as many times as needed to achieve a score of 100%.
4. After successfully completing the last test of the semester, your browser will be automatically directed to the activity evaluation form, which you will submit online.
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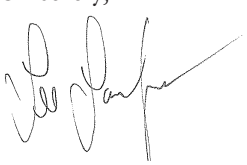
This activity is valid 36 months from the date of publication for ACCME credit and 12 months from the date of publication for AAFP credit. The target audience for this activity includes internist/family physicians.

If you have any questions about the process, please call us at (800) 688-2421, or outside the U.S. at (404) 262-5476. You can also fax us at (800) 284-3291, or outside the U.S. at (404) 262-5560. You can also email us at: customerservice@ahcmedia.com.

On behalf of AHC Media, we thank you for your trust and look forward to a continuing education partnership.

Sincerely,



Lee Landenberger
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