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Internal Medicine

Evidence-based summaries of the latest research in internal medicine [ALERT]

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ABSTRACT & COMMENTARY

Antibiotic Use and Risk of Diabetes

By Seema Gupta, MD, MSPH

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

SYNOPSIS: In a population-based, case-control study of incident type 2 diabetes cases, researchers found that more frequent users of antibiotics were more likely to be diagnosed with type 2 diabetes than those who had taken the drugs infrequently.

SOURCE: Mikkelsen KH, et al. Use of antibiotics and risk of type 2 diabetes: A population-based case-control study. *J Clin Endocrinol Metab* 2015;100:3633-3640.

Since their discovery in the 1920s, antibiotics have transformed our ability to manage infectious diseases. Today, antimicrobials are one of the most commonly prescribed medication classes in the United States. However, it is estimated that more than half of antibiotics prescribed for patients visiting a clinic are inappropriate. In fact, more than 25% of prescriptions are for conditions for which antibiotics are rarely indicated and tend to be more often broad-spectrum.[1] Substantial evidence indicates that many prescriptions are for viral illnesses, for which antibiotics provide no benefit.[2] Similarly, 30-50% of antibiotic use in hospitals is unnecessary or inappropriate. Considerable geographical variation in outpatient antibiotic prescribing rates has been observed. The inappropriate use and overuse of antibiotics are major drivers of antibiotic resistance, leading to a significant public health threat. Each year in the United States, at least 2 million people become infected with bacteria that are resistant to antibiotics and at least 23,000 people die as a direct result of these infections. In addition, antibiotics cause one out of five emergency department visits for adverse drug events (ADEs) and are the most frequent cause of ADEs in children.[3,4]

Similar to the antibiotic issue, type 2 diabetes mellitus (T2DM) also represents a major public health challenge, in large part due to the rising epidemic of obesity. T2DM is associated with significant

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comorbidities and healthcare costs. The latest research suggests that microbes that colonize the human gut may play key contributory roles to the development of obesity and metabolic syndromes, such as T2DM.[5] Since antibiotics also cause marked alterations in the human gut microbiota, some observational studies have linked exposure to antibiotics with the development of obesity.[6]

Mikkelsen et al conducted a population-based, case-control study to investigate whether the use of antibiotics influences the risk of developing T2DM. The researchers utilized three national registries in Denmark to track patients' antibiotic prescriptions between 2000 and 2012: 170,504 who had T2DM and 1.36 million who did not.

Researchers found that T2DM patients treated filled on average 0.8 antibiotic prescriptions per year compared to 0.5 prescriptions per year among controls. The more antibiotics patients utilized, the more likely they were to have T2DM. Compared with having filled none to one prescription for antibiotics, those who filled two to four prescriptions had a 21% higher risk (95% confidence interval [CI], 1.19-1.23) for T2DM, and those who filled five or more had a 53% higher risk (95% CI, 1.50-1.55). Slightly higher odds ratios were found for narrow-spectrum and bactericidal antibiotics compared with broad-spectrum and bacteriostatic antibiotics, respectively. The increased use of antibiotics in patients with T2DM was found up to 15 years before diagnosis of T2DM as well as after the diagnosis.

■ COMMENTARY

This study seems to support findings of others in the field that an increased risk for developing T2DM may occur with more exposure to antibiotics. Indeed, several studies suggest that antibiotics may drive changes in glucose homeostasis, insulin sensitivity, and adipose tissue metabolism by altering the gut microbiota.[7] Antibiotics have been traditionally used in agriculture to achieve weight gain in livestock. However, it is also important to consider another possibility. Patients with T2DM are more susceptible to infections and may naturally take more antibiotics. The study demonstrates that these patients may be more prone to developing infections many years before they become diagnosed with T2DM. This may be attributed to developing an increased risk of infections during pre-diabetes, a condition often co-existing with being overweight or obese, which precedes T2DM development. While the study demonstrates an association between antibiotic use and T2DM, it does not establish a causation, and further research is needed. However, it provides another possible reason why we should be leaders in promoting antimicrobial stewardship in order to optimize antibiotic use for achieving the best clinical outcomes while minimizing adverse events and the emergence of resistance. ■

[This study provides another possible reason why we should be leaders in promoting antimicrobial stewardship in order to optimize antibiotic use for achieving the best clinical outcomes while minimizing adverse events.]

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ABSTRACT & COMMENTARY

Eat Right, Preserve Your Memory, and Stay Happy

By Joseph E. Scherger, MD, MPH

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

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

SYNOPSIS: Greater intake of unhealthy food and lower intake of nutrient-dense food is associated with a smaller hippocampus over 4 years in adults 60-64 years of age.

SOURCE: Jacka FN, et al. Western diet is associated with a smaller hippocampus: A longitudinal investigation. *BMC Medicine* 2015;13:215-222.

A team of investigators from Australia used a database of 2551 adults living in and around Canberra who participated in the Personality and Total Health (PATH) Through Life project starting in 2001. A subgroup of 255 patients were in the age 60-64 cohort and had both a diet survey and an MRI initially, then 4 years later. Diets were self-reported and put on a scale from "prudent" (healthy) emphasizing fresh vegetables, salad, fruit, and grilled fish to "Western" (unhealthy) emphasizing roast meat, sausages, hamburgers, steak, chips, and soft drinks.

Significant differences were found with diet and change in the size of the hippocampus on MRI. Every 1 standard deviation increase in the healthy dietary pattern was associated with a 45.7 mm larger left hippocampal volume, while a higher consumption of the unhealthy foods was independently associated with a 52.6 mm smaller left hippocampal volume. These relationships were independent of variables such as age, gender, education, work status, depressive symptoms, medication, physical activity, smoking, hypertension, and diabetes.

This is the first study that demonstrated a relationship between diet and the size of the hippocampus in humans. Such an association has been shown in animals.[1,2] The authors proposed a variety of mechanisms for this change, such as inflammation, oxidative stress, and the gut microbiome.

■ COMMENTARY

The hippocampus is a part of the brain associated with learning, memory, and mood regulation. The hippocampus has been specifically implicated as a site for depression.[3] Environmental factors, especially nutrition and physical activity, have been shown to reduce or increase through neurogenesis the size of the hippocampus.[4] This study shows that just 4 years in the sixth decade makes a significant difference in the size of the hippocampus, depending on diet.

I recently read an amazing book, *The Story of the Human Body*, by the Harvard evolutionary biologist Daniel Lieberman.[5] Lieberman traces the development of humans from the chimpanzee through the hominoids to our long hunter-gatherer period. He then describes the impact of the agrarian and industrial ages on our bodies and our health. The impact has been mostly negative. Sure, we are living longer than ever (for now), but we have a multitude of diseases not known to the animal kingdom. Most importantly, we have a growing epidemic of cognitive impairment and dementia.

Nutrition may have a preeminent role in the health of our brains. The emergence of understanding the gut microbiome in brain health has been presented in *Internal Medicine Alert* recently.[6] Inflammation appears to be the common denominator in most chronic diseases involving the body and mind. Unhealthy foods induce inflammation in the body, something that deserves much more attention in our social policies, public health, and medical practice. ■

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ABSTRACT & COMMENTARY

Eat Breakfast, Fix Insulin Resistance in Patients with Type 2 Diabetes

By Jeff Unger, MD, FACE

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Dr. Unger reports that he participates on the speaker's bureau for Janssen Pharmaceuticals, Novo Nordisk, and Valeritas; is an advisory board member for Janssen, Sanofi-Aventis, Novo Nordisk, Halozyme, and Abbott; is a consultant for Novo Nordisk, Sanofi-Aventis, Valeritas, and Dance Pharmaceuticals; and receives research/grant support from Boehringer Ingelheim, Novo Nordisk, GSK, Eli Lilly, Johnson and Johnson, Pfizer, Sanofi-Aventis, Takeda, and Merck.

SYNOPSIS: Skipping breakfast increases lunch and dinner postprandial glucose levels due to impaired GLP-1 secretion. The resultant escalation of insulin resistance can have an impact on long-term diabetes management. Breakfast consumption could be a successful strategy for reducing postprandial hyperglycemia in patients with type 2 diabetes.

SOURCE: Jakubowicz D, et al. Postprandial hyperglycemia and impaired insulin response after lunch and dinner in individuals with type 2 diabetes: A randomized clinical trial. *Diabetes Care* 2015;38:1820-1826.

Twenty-six patients with type 2 diabetes, duration < 10 years, and an A1c 7-9 % were recruited for this randomized, open-label, crossover-within-subject clinical trial in Venezuela. Patients served as their own controls. None of the patients worked graveyard shifts, and all woke up between 6 a.m. and 7 a.m. and went to sleep between 10 p.m. and 11 p.m. nightly. Patients were insulin- and GLP-1 receptor agonist-naive and taking only metformin. Participants underwent two separate all-day meal tests with a washout of 2-4 weeks between testing days. On the day participants ate breakfast, three identical standard meals were provided in the clinic at planned times. On days when breakfast was not consumed, lunch and dinner were provided on the same schedule. Blood samples were obtained from all participants at 15, 30, 60, 90, 120, 150, and 180 minutes after eating commenced for each meal. The primary outcome was the assessment of postprandial glycemia following lunch and dinner in patients who ate or skipped breakfast. Secondary outcomes were the assessment levels of plasma insulin, C-peptide, intact GLP-1 (iGLP-1), free fatty acid, and glucagon.

When skipping breakfast, the peaks of plasma glucose after lunch and dinner were 39.8% and 24.9% higher, respectively. Skipping breakfast resulted in a 1-hour delay of iGLP-1 secretion and a 21.5% lowered peak response at lunch, compared with levels obtained when breakfast was consumed. Skipping breakfast induced insulin resistance by increasing levels of glucagon, free fatty acids, reducing endogenous insulin secretion, and iGLP-1 following lunch and dinner. Eating breakfast reversed this adverse metabolic state.

■ COMMENTARY

In type 2 diabetes, postprandial hyperglycemia has a significant effect on A1c and long-term outcomes. Reducing peaks in post-meal glucose levels may slow the progression of beta-cell function and improve microvascular and macrovascular disease. From a clinical perspective, many of our patients believe that skipping breakfast will result in a reduction in caloric consumption during the day. However, upon careful examination of their glucose logs, these patients actually have a rise in glucose levels beginning mid-day, which continues until bedtime. Breakfast has been demonstrated to be of major importance for the 24-hour regulation of glucose. Skipping breakfast has been associated with weight gain, increased insulin resistance, and an increased risk of developing type 2 diabetes. The omission of breakfast in patients with type 2 diabetes is associated with a significant rise in A1c and all-day postprandial hyperglycemia. Most of the metabolic pathways involved in postprandial glycemia, including beta-cell secretory function, insulin sensitivity, muscle glucose uptake, muscle glycogen storage, and hepatic glucose production, are controlled by the circadian clock. Skipping breakfast, therefore, has a tremendous metabolic impact on insulin resistance.

Based on the findings of this well-controlled study, patients with type 2 diabetes should be instructed that the consumption of breakfast will likely result in a reduction in postprandial hyperglycemia, improvement in GLP-1 secretion, and a decrease in overall insulin resistance. ■

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ABSTRACT & COMMENTARY

Treatment for Ulnar Neuropathy at the Elbow

By Michael Rubin, MD

Professor of Clinical Neurology, Weill Cornell Medical College

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

SYNOPSIS: In a randomized treatment trial of steroid injection into the cubital tunnel for ulnar neuropathy, there was no difference in outcome compared to placebo.

SOURCE: vanVeen KEB, et al. Corticosteroid injection in patients with ulnar neuropathy at the elbow: A randomized, double-blind, placebo-controlled trial. *Musc Nerve* 2015;52:380-385.

Conservative management for ulnar neuropathy at the elbow (UNE) is preferable to surgical treatment, and includes splinting or padding the elbow, modification of activities, avoiding provocative factors, and nerve gliding exercises. However, none of these conservative treatments are of proven benefit. In a Cochrane review of randomized or quasi-randomized controlled clinical trials, no difference was found between simple decompression and transposition of the ulnar nerve for either clinical or neurophysiological improvement,[1] and in the single trial evaluating conservative treatments, night splinting and nerve gliding exercises added no benefit over simply avoiding prolonged movements or positions. Are glucocorticoid injections, often used for carpal tunnel syndrome, of any benefit for UNE?

In this randomized, double-blind, placebo-controlled trial, patients with UNE seen at the Medical Center Haaglanden, The Hague, between September 2009 and April 2014, were recruited for evaluation. Inclusion criteria comprised motor or sensory symptoms of ulnar neuropathy, coupled with positive electrodiagnostic or ultrasonography findings for UNE, with patients excluded if they were < 18 years of age, had a history of prior ulnar nerve subluxation or UNE, were taking oral corticosteroids or anticoagulants, or had prednisolone allergy. Electrodiagnostic criteria for UNE required either motor nerve conduction velocity (MNCV) across the elbow slower than 43 m/s, slowing of MNCV across the elbow by more than 15 m/s compared to the forearm segment, or motor conduction block across the elbow of greater than 16%, comparing above to below elbow stimulation. Ultrasonography (US) was considered positive for UNE if the cross-sectional area (CSA), examined in perpendicular planes from at least 2 cm proximal to 2 cm distal to the medial epicondyle was > 10 mm. Patients were randomized to receive, by US guided injection, 1 mL containing either NaCL 0.9% or 40 mg depo-medrol (methylprednisolone acetate and 10 mg lidocaine hydrochloride). Subjective improvement at 6 months, as defined by a 6-point scale, was the primary outcome measure, with changes in electrodiagnostic studies and US findings comprising the secondary outcome measures. Statistical analysis included the chi-square test, the Mann-Whitney U-test, and Wilcoxon signed rank test.

Among 63 patients included in the study, which was halted due to slow recruitment, five were lost to follow-up, leaving 27 men and 28 women, with a mean age of 55 years, for analysis. No significant difference was found between the treatment vs placebo groups for either the primary or electrodiagnostic secondary outcome. Nerve CSA decreased significantly in the depo-medrol group, from 11.9 mm^2 to 10.9 mm^2. Neither symptoms nor neurological findings differed, comparing findings at 3 months to those at study initiation. Four depo-medrol patients reported complications, including hand swelling or pain, swelling, or depigmentation at the injection site, compared to one patient in the placebo group with pain at the injection site. US-guided corticosteroid injection in UNE is no better than placebo.

■ COMMENTARY

What causes ulnar neuropathy at the elbow? Among 117 patients with confirmed UNE, prospectively recruited, and seen by four blinded examiners who each performed separate neurologic evaluations and electrodiagnostic and ultrasound studies, 73% and 27% had lesions at the retro-epicondylar groove (REG) or under the humero-ulnar aponeurosis (HUA), respectively. HUA ulnar neuropathy was associated with manual labor, dominant arm involvement, and

older age, whereas REG ulnar neuropathy was due to compression, mainly affecting the non-dominant arm of younger administrative personnel. These findings may assist in the prevention of UNE. ■

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PHARMACOLOGY UPDATE

Idarucizumab Injection (Praxbind)

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

Dr. Elliott is Medical Director, Pharmacy, 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. Elliott and Chan report no financial relationships relevant to this field of study.

The FDA has approved the first reversal agent for a direct oral anticoagulant (DOAC). Idarucizumab is a humanized monoclonal antibody fragment derived from an IgG1 isotype molecule. The monoclonal antibody directly binds to dabigatran (Pradaxa), rapidly neutralizing its pharmacologic effect. The drug was approved under the FDA's accelerated approval process. It is marketed as Praxbind by Boehringer Ingelheim.

INDICATIONS

Idarucizumab is indicated in patients treated with dabigatran when reversal of the anticoagulant effect is needed.[1]

DOSAGE

The recommended dose is 5 g given as two consecutive intravenous infusions or as two consecutive bolus injections.[1] Idarucizumab is available as 2.5 g vials.

POTENTIAL ADVANTAGES

Idarucizumab effectively reverses the anticoagulant effect of dabigatran[1,2] and has minimal side effects.

POTENTIAL DISADVANTAGES

Reversing the effect of dabigatran exposes patients to thromboembolic risk of their underlying disease.[1] Elevated coagulation parameters have been observed between 12 and 24 hours after administration.[1] Treatment-emergent, possibly persistent anti-idarucizumab antibodies were observed in 4% of subjects. The formulation contains sorbitol; thus, there is a risk of serious reaction in patients with hereditary fructose intolerance.[1]

COMMENTS

The safety and efficacy of idarucizumab was evaluated in three trials in healthy volunteers (n = 283) and in one study in subjects taking dabigatran who received idarucizumab due to uncontrolled bleeding or requiring emergency surgery (n = 123, with n = 90 evaluable). Compared to placebo, the infusion of idarucizumab significantly reduced coagulation parameters (dTT, aPTT, ECT, TT, and ACT) at the end of the infusion. Reductions ranged from 51%-90% compared to no change for placebo. In the second study, subjects were divided into two groups. Fifty-one had serious bleeding (Group A) and 39 required an urgent procedure (Group B). The primary endpoint was the maximum percentage reversal of anticoagulation effect at any point from the end of the first infusion to 4 hours after the second administration. The median maximum percent reversal was 100%. The effect was evident within minutes. The secondary endpoints included the proportion of subjects who had complete normalization of the dilute thrombin time or ecarin clotting time in the first 4 hours and reduction in the concentration of unbound dabigatran. Dilute thrombin time was normalized in 98% of Group A and 93% in Group B and 89% and 88%, respectively, for ecarin clotting time.[2] At 4 hours, 97% had dabigatran levels near the lower limit of quantification. Of the subjects in group B who underwent a procedure, 33 reported normal intraoperative hemostasis restored, with two mildly and one moderately abnormal. Thrombotic events occurred in five subjects ranging from 2 to 26 days after treatments. There were 18 deaths overall, with 10 due to vascular causes and five due to fatal bleeding events.[2] Ten fatalities occurred within 96 hours of idarucizumab and the remaining ranged from 4 to 101 days. Early deaths appear to be related to the index event and later deaths to coexisting conditions.[2] There is redistribution of dabigatran 12 hours after idarucizumab administration from extravascular compartment into the intravascular compartment.

CLINICAL IMPLICATIONS

Idarucizumab is the first agent to effectively reverse the anticoagulant effect of a DOAC. Lack of a rever-

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Clinical Briefs

By Louis Kuritzky, MD

Difficult Choices in Long-term Osteoporosis Management

SOURCE: Leder BZ, et al. Denosumab and teriparatide transitions in postmenopausal osteoporosis (the DATA-Switch study): Extension of a randomised controlled trial. *Lancet* 2015;386:1147-1155.

The propriety of long-term bisphosphonate utilization (that is, > 5 years) has recently come into question subsequent to a clinical trial that compared bisphosphonate discontinuation at 5 years vs continuation for 10 years. Despite a decline in bone mineral density (BMD) in the cessation group, the actual hip fracture rate was no greater than in the group that continued bisphosphonate for 10 years. Since there are adverse effects and expense associated with treatment, many questions remain about how long to treat and which agent(s) to utilize.

In the DATA (Denosumab and Teriparatide Administration) trial, postmenopausal women (n = 94) with osteoporosis were randomized to treatment with teriparatide (TER), denosumab (DEN), or both for 2 years. DATA-Switch is an extension of DATA, during which patients on monotherapy were switched (e.g., if on DEN for 2 years, switched to TER, and vice versa), and patients on dual therapy (DEN + TER) were switched to DEN monotherapy. The SWITCH phase of the trial lasted an additional 2 years. TER patients switched to DEN, and DEN + TER patients switched to DEN monotherapy continued to accrue more mass at the lumbar spine, distal radius, femoral neck, and total hip. Women who were switched from DEN to TER lost BMD at the distal radius, and showed losses of BMD in the femoral neck and total hip for the first 12 months, after which some gain in BMD occurred.

Ultimately, the greatest improvements in BMD were seen in women who were assigned initially to DEN + TER and then switched to DEN monotherapy. Hopefully, we will see similar trials in the future to guide us in switching between bisphosphonates and alternative agents such as denosumab. ■

ACE Inhibitors vs ARBs for Hypertension

SOURCE: Kaplan NM. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers for hypertension: Are they equivalent? *J Am Soc Hypertens* 2015;9:582-583.

Recommendations from the panel assigned to develop Eighth Joint National Committee hypertension guidelines indicate that angiotensin-converting-enzyme (ACE) inhibitors and angiotensin II receptor blockers (ARBs) (as well as thiazide-type diuretics and calcium channel blockers) are all appropriate initial therapies for hypertension in the general non-black population. For persons with chronic kidney disease and hypertension, this same document suggests ACE inhibitors or ARBs, without distinction. But should we consider ACE inhibitors and ARBs essentially interchangeable? An editorial review of this issue in the *Journal of the American Society of Hypertension* suggests otherwise, preferring ACE inhibitors over ARBs both in the general population and persons with diabetes.

The endorsement for ACE inhibitors over ARBs by this editorialist does not stem from a large randomized trial comparing the two. Rather, meta-analyses of a large number of hypertension trials has shown that whereas ACE inhibitors consistently reduced cardiovascular mortality, including myocardial infarction, ARBs do not demonstrate the same convincing risk reduction, especially for myocardial infarction. Since a large randomized trial comparing ACE inhibitors to ARBs is highly unlikely in the near future, if at all, this data review would support using ACE inhibitors preferentially over ARBs in most patients with hypertension. ■

Uric Acid as a Predictor of Hypertension

SOURCE: Leiba A, et al. Uric acid levels within the normal range predict increased risk of hypertension: A cohort study. *J Am Soc Hypertens* 2015;9;600-609.

Currently accepted laboratory standards indicate that the upper limit of "normal" for uric acid levels is 7 mg/dL in men and 6 mg/dL in women. Uric acid has been recognized as a cardiovascular risk factor for more than 3 decades, thanks to data from the Framingham study. Nonetheless, whether uric acid causes — or is simply associated with — adverse cardiovascular outcomes is uncertain. Additionally, even if the association of uric acid with cardiovascular disease is determined to be causal, it will remain necessary to definitively prove that reductions in uric acid improve outcomes (without undue risk).

Using analysis from the largest HMO in Israel, healthy adults aged 40-70 years (n = 118,920) had baseline uric acid levels obtained in 2002, and were subsequently followed for 10 years. During this interval, almost one-quarter of these had a new diagnosis of hypertension recorded. The risk of hypertension in women and men began to increase well within the "normal" range. Compared to a uric acid of 2-3 mg/dL, even patients with uric acid of 3-4 mg/dL were 15% more likely to become hypertensive; higher "normal" uric acid (5-6 mg/dL) was associated with a 66% increased incidence of hypertension. Results were similar for both women and men. The authors suggested that our currently defined levels of "normal" for uric acid may have to be reconsidered. ■

Continued from page 22

sal agent has been seen as a major drawback for administration of these drugs, especially in individuals who may be at higher risk of bleeding or falls. A reversal agent for the Xa inhibitors (rivaroxaban, apixaban, edoxaban) is in Phase 2 trials. Meanwhile, approval of idarucizumab gives Boehringer Ingelheim a marketing advantage for dabigatran over other DOACs. The wholesale cost is $3500 for a single administration (5 g). ■

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CME QUESTIONS

1. Based on the study by Mikkelsen et al, researchers found that frequent users of antibiotics had:

a. more likelihood of developing type 2 diabetes mellitus.

b. less likelihood of developing type 2 diabetes mellitus.

c. more likelihood of developing obesity.

d. less likelihood of developing obesity.

2. A reduction in the size of the hippocampus is associated with what nutritional habit?

a. Eating lots of nuts and seeds

b. Eating lots of vegetables and fruit

c. Eating lots of seafood

d. Eating lots of meats, such as sausages and hamburgers

3. Skipping breakfast will result in all of the following metabolic changes *except*:

a. a rise in intact GLP-1.

b. a rise in post prandial glucose during lunch and dinner.

c. a rise in plasma glucagon levels during lunch and dinner.

d. an increase in plasma free fatty acid levels.

e. a reduction in serum insulin levels.

4. Which of the following therapies have been shown, by double-blind, placebo-controlled trial, to be beneficial for ulnar neuropathy at the elbow?

a. Splinting or padding the elbow

b. Modification of activities

c. Nerve gliding exercises

d. Corticosteroid injection into the elbow

e. None of the above

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]

Risk Of New Onset Diabetes When Blood Pressure Becomes Elevated Over the Usual Blood Pressure