Answers to your questions from our medical experts

1. What's the deal with low-carb diets?

Why is there loss of body weight when carbohydrates are reduced if the total caloric intake remains constant?

Submitted by:
Bill Macke, MD
Vancouver, British Columbia

A calorie is still just a calorie! Many controlled trials have documented that there is no weight loss difference between same-calorie diets, regardless of the amount of proteins vs. carbohydrates.

Recently, one large trial compared daily intake of < 60 g of carbohydrates to daily intake of > 60 g and showed that weight loss was predicted by the reduced calorie intake, longer durations and greater pre-diet weights.[1]

Possible explanations for physical changes with low-carbohydrate diets include:

1. Adherence to the prescribed diets (*i.e.*, reduced carbohydrate diets are easier to follow, at least in the short term).

2. Much of the rapid weight loss in a low-carbohydrate diet is diuresis due to the diuretic effect of ketone bodies. These diets tend to be restrictive and generate ketosis. Mobilization of glycogen stores may also contribute to diuresis.

3. Higher protein diets are associated with increased satiety and a reduced caloric intake, by almost 500 kcal/day, on average.[2]

References
1. Bravata DM, Sanders L, Huang J, et al: Efficacy and safety of low-carbohydrate diets: A systematic review. J Am Med Assoc 2003; 289(14):1837-50.
2. Bray GA: Low carbohydrate diets and realities of weight loss. JAMA 2003; 289(14):1853-5.

Answered by:
Karri Koach RD, CDE
Lifestyle Metabolism Centre
Oakville, Toronto and Thornhill, Ontario

This month's topics:

2. ACTH, cortisol and depression

How do high levels of adrenocorticotropic hormone (ACTH) and cortisol cause depression and panic?

Submitted by:
Barbara Powell, MD
Kanata, British Columbia

Pathologic alterations in hypothalamic-pituitary-adrenal function have been associated primarily with mood disorders and post-traumatic stress disorders. Cushing's syndrome has been associated with mania, depression and psychosis. The exact mechanism is not known, however, the finding that corticosteroids have multiple regulatory effects on serotoninergic functions, particularly on the serotonin subtype 1A receptor, may be relevant, as may be the state-dependent, stimulant-like effects that glucocorticoids can exert on mesencephalic dopamine transmission.

Answered by:
Hany Bissada, MD, FRCP(C)
Director, Regional Centre for the Treatment of Eating Disorders
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Ottawa, Ontario

3. Guidelines for clopidogrel

What are the current recommendations on using clopidogrel for longer than one month in:

a) a patient who had a stent for single-vessel coronary disease; or

b) a patient who has multivessel coronary disease with a stent and multiple risk factors?

Submitted by:
B.L. Chandrarajan, MD, CCFP
Kingston, Ontario

Patients receiving bare metal stents should be treated with acetylsalicylic acid (ASA) and clopidogrel for at least 28 days to minimize risk of stent thrombosis. Combination therapy should continue for at least three months if a sirolimus-eluting stent is used and for at least six months if a paclitaxel-eluting stent is used (because of concerns about delayed re-endothelialization with drug-eluting stents).

Whether both ASA and clopidogrel should be continued for longer than this is controversial and not clearly guided by randomized clinical trials.

Patients at high risk of adverse cardiac events (*e.g.*, those who initially present with an acute coronary syndrome or who are known to have widespread vascular disease) should certainly be considered for longer-term combination therapy. In this context, combination therapy should continue for nine to 12 months following percutaneous coronary intervention, but potentially even longer if the risk of recurrent events remains high.

Bleeding complications related to combination therapy can be minimized by using the lowest possible dose of ASA.

Answered by:
Michael Love, MD, MB, ChB
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4. Chlamydia testing

How would you compare urine testing with vaginal swabs for diagnosing genital chlamydia infection?

Submitted by:
Parvinder Singh, MD
Markham, Ontario

Nucleic acid amplification of a cervical swab for chlamydia trachomatis is more sensitive than testing a urine specimen. In one study, the sensitivities of testing cervical swabs using ligase chain reaction or polymerase chain reaction were 91.4% and 84.0%, respectively when compared to a culture specimen from the cervix. The sensitivities were slightly lower when using these reactions on urine specimens.[1] Similar results have been found in males.[2]

Having a very sensitive test becomes even more important in populations where there is a low incidence of infection, as a greater proportion of patients who are infected will otherwise be missed.

The swab can, however, be invasive and patients are less likely to have testing done. In this situation, either a urine or self-collected vaginal specimen are perfectly acceptable alternatives.

References
1. Black CM, Marrazzo J, Johnson RE, et al: Head-to-head multicenter comparison of DNA Probe and nucleic acid amplification tests for chlamydia trachomatis infection in women performed with an improved reference standard. J Clin Microbiol 2002; 40(10):3757-63.
2. Johnson RE, Green TA, Schachter J, et al: Evaluation of nucleic acid amplification tests as reference tests for chlamydia trachomatis infections in asymptomatic men. J Clin Microbiol 2000; 38(12):4382-6.

Answered by:
James Graham, MD, FRCSC
Division of reproductive endocrinology and infertility
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5. Calculating cardiac risk

Does the Framingham data reflect ECG evidence of LVH or true LVH documented on echocardiogram? How should we calculate the risk in the presence of this contradictory lab data?

Submitted by:
Stuart Glaser, MD, CCFP, FCFP
Montreal, Quebec

The Framingham cardiovascular risk calculation was based on electrocardiogram (ECG) evidence of left ventricular hypertrophy (LVH). Although, the ECG in most settings is < 40% sensitive to the presence of LVH, it is nevertheless quite specific.

The echocardiogram is the gold standard clinical test and is both sensitive and specific. If ECG is normal, but echocardiogram shows LVH, the patient's risk is increased.

Although the Framingham risk score has not been validated using echocardiography, the patient's risk calculation should include data from echocardiography when available. However, echocardiograms are not recommended to routinely assess LVH in patients with hypertension.

Interestingly, recent data has suggested that both ECG and echocardiogram provide data on LVH that are independently prognostic. Patients with ECG evidence of LVH and normal echocardiograms appear to be at higher risk.

Answered by:
Norman Campbell, MD, FRCPC
Professor, faculty of medicine
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Calgary, Alberta

6. CCB/ACE inhibitor combinations

Other than compliance, what is the rationale for using CCB/ACE inhibitor combined tablets?

Submitted by:
Stephen Coyle, MD, MBBS, LMCC
Winnipeg, Manitoba

Randomized studies suggest patients often need between two and four drugs to achieve target blood pressure (BP). If initial BP is > 20/10 mmHg beyond target, the Joint National Committee even recommends patients be immediately started on two medications.

Combination therapy synergistically interferes with pathogenetic mechanism (renin-angiotensin-aldosterone system with angiotensin-converting enzyme [ACE] inhibitors; all antagonists and beta blockers; volume-dependant hypertension with diuretics and calcium channel blockers [CCBs]).

Further, the use of lower doses of each agent diminishes compensatory stimulation and limits toxic effects, as one agent may counteract some deleterious effects of the other. Lower drug acquisition costs is also of benefit.

Specifically, CCBs have a natriuretic effect that may potentialize ACE inhibitors and, thus, may obviate the need for a diuretic when desirable. ACE inhibitors have been shown to reduce the edema associated with CCBs.

Beyond the well-proven protection of ACE inhibitors in atherosclerotic heart disease, there is also a wealth of basic lab data suggesting CCBs may help prevent arteriosclerosis in addition to being excellent antianginal agents. What's more, both classes are successful against left ventricular hypertrophy, so their combination is particularly effective.

Some recent studies have addressed this issue. The combination of amlodipine and benazepril has been evaluated in two different studies: ALERT and SELECT. In both cases, the combination was associated with greater BP reductions than either agent alone.

Answered by:
Michel Samson, MD
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7. Detecting bipolarity

In a depressed person, what clues can lead to the diagnosis of bipolarity? Can a trial of SSRI lead to a manic episode?

Submitted by:
Waguih Tannous, MD
Montreal, Quebec

Bipolar depression is misdiagnosed as unipolar depression more than 50% of the time and the diagnosis is often not made until the occurrence of a manic episode. Episodes of bipolar depression tend to be more frequent, of faster onset and of shorter duration than in unipolar depression.

Current evidence suggests that although antidepressants are clearly effective in the acute treatment of bipolar depression, they can induce a switch to mania at a rate two or three times the spontaneous rates; long-term use can destabilize the illness, leading to cycle acceleration and mixed mood states, particularly in the absence of a mood stabilizer such as lithium. Overall, the tricyclic and monoamine oxidase inhibitor antidepressants are associated with greatest risk of manic switch with a slightly elevated risk for selective serotonin reuptake inhibitors; bupropion and mirtazapine appear to be associated with the least risk.

Answered by:
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Edmonton, Alberta

8. Are Pap smears effective?

Are Pap smears as effective as internal exams? Which patients should have internal exams (*i.e.*, what age group)?

Submitted by:
Wayne Dong, MD, CCFP
Valemount, British Columbia

I would recommend considering Pap smear and pelvic exam as two distinct investigations.

Pap smear, carried out annually, is a highly effective method of screening for the prevention of cervical cancer. The current rates of Pap smear use in Canada are low. It is critical that family doctors push to ensure patients have regular screening.

Regarding pelvic exam, I recommend it be carried out annually at the time of gynecologic checkup. This exam includes careful inspection of the vulva and vagina, followed by bimanual palpation of the uterus and adnexa, as well as Pap smear. This process should be done regularly for all women once they are sexually active.

It is very important that pelvic exam be carried out in any woman who presents with abdominal complaints, as ovarian cancer may often present with non-specific symptoms, such as:

- abdominal distention,
- bloating or
- vague pain.

No single method of effective screening for ovarian cancer has been proven to date.

Answered by:
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9. Pneumococcal vaccine for diabetes patients?

Is there any role for pneumococcal vaccine in otherwise well patients with diabetes?

Submitted by:
Diane Zatelny, MD
Barrie, Ontario

Patients with Type 2 diabetes have an increased risk of pneumococcal infections and experience increased morbidity and mortality when infected, compared to the general population.

Various abnormalities in the host defense mechanisms, such as poor antibody response, altered cell-mediated immunity and altered leukocyte function have been proposed to confer this increased risk.

Randomized clinical trials of pneumoccocal vaccination in patients with diabetes have not been performed for obvious ethical reasons, but the available evidence suggests vaccination is effective in reducing invasive pneumococcal disease. There is, however, uncertainty of vaccine efficacy in non-bacteremic pneumococcal infections.

Both the Canadian and the American Diabetes Associations recommend pneumococcal vaccination in all patients with diabetes. Revaccination is recommended for individuals over 65 years old if the original vaccine was administered when they were under 65 and if it was administered more than five years earlier.

Answered by:
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10. Side-effects of chemotherapy

What can I do to help patients receiving chemotherapy who get oral ulcers?

Submitted by:
Shelly Smith, MD, CCFP
Edmonton, Alberta

Chemotherapy often results in erythema, atrophy and ulceration of the oral mucosa, generally referred to as oral mucositis (OM). It is estimated that some degree of OM occurs in approximately 40% of patients receiving chemotherapy.

Treatment is symptomatic, as OM is normally self-limited. Considerations are:

1. Oral debridement: Normal saline on a Q-tip or baking soda mouth washes (1 teaspoon in 8 oz. cool water) help remove oral debris.
2. Oral decontamination:
   - Mouth washes with chlorhexidine can be helpful.
   - If necessary, treat secondary *Candida albicans* with nystatin rinses (swish and swallow) or clotrimazole troches.
   - Oral fluconazole can be used in severe cases.
   - Secondary herpes simplex should be treated with oral antiviral agents such as famciclovir or valacyclovir.
3. Topical and systemic pain management: Viscous lidocaine hydrochloride, 2%, rinses can give symptomatic relief from pain.

Topical sucralfate rinses (to form a viscous adhesive layer to protect oral mucosa) have been tried, although several recent studies show no benefit over placebo.

Answered by:
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11. Diagnosing drug allergy

What is the safest and most accurate way of confirming or refuting a supposed drug allergy in which there is no documented allergic reaction and the patient has no memory of the reaction?

Submitted by:
Declan Boylan, MD, FRCPC
Sudbury, Ontario

In short, there is no direct way to confirm or refute a supposed drug allergy when no history is available. Diagnosis of drug allergy is largely clinical and not based on specific lab or skin tests.

In the case of penicillin, immune response determinants have been characterized, thus, standardized intradermal skin testing can be done. For most other drugs, relevant metabolites and the precise immunologic mechanisms are not known. In many cases, reactions may be the result of multiple mechanisms.

It is the nature, onset and evolution of symptoms that define the likelihood of a drug allergy. In the case of possible immunoglobulin (Ig)E-mediated reactions to penicillins, skin testing can help verify or refute an allergy, as part of an entire assessment. Skin tests may be useful with some other medications (only for IgE-mediated reactions), but this approach has not been standardized.

In any individual patient, there would be no quick and accurate way to verify the presence/absence of a drug allergy. Most mild morbilliform reactions that occur in early childhood are likely the result of a concomitant infection, or an infection/drug cofactor effect. These reactions tend not to recur with future exposure. Even in documented IgE-mediated reactions to penicillins, the vast majority of patients become tolerant within 10 years.

If the reaction-inducing drug is considered vital for the patient, an oral challenge can be considered, either alone or as part of a desensitization protocol. The desensitization would have to be done under expert supervision in a setting where resuscitation equipment is readily available. D_x

Answered by:
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