Answers to your questions from our medical experts

1. Female partners and Paps

Is it necessary to perform regular Paps on married female patients with a low risk of STD contraction? If they have had three negative Pap tests by age 40, could they have the next one at age 60 instead of 50?

Submitted by:
Grah...

Current recommendations for the programmatic screening for cervical cancer are: After two satisfactory Paps taken a year apart, the frequency can be reduced to every three years until age 69 in low-risk women.[1] This applies to women without a history of human papillomavirus in themselves or their partner, current smoking, sexu...

...asive ...med at one-, two- ...low-risk women.[2] In addition, ...diagnosed, invasive cervical cancers are in ...omen who have never had a Pap or have not had a Pap in more than five years.[3] After 70 years of age, Pap smears can be discontinued in women with a history of normal cytology.

This month's topics:

References
1. Cervical cancer prevention network. Quality Management Working Group. Programmatic guidelines for screening for cervical cancer in Canada. Ottawa, Ont. Health Canada and Society of Gynecologic Oncologists of Canada; 1998.
2. Lotocki RJ: The Pap Smear: Guidelines for screening and follow-up. The Can J CME 2000; 12(12):147-58.
3. Anderson GH, Banadet JL, La Riche JC, et al: Invasive Cancer of the Cervix in British Columbia: A review of the demography and screening histories of 437 cases seen from 1985 to 1988. Obstet Gynecol 1992; 80(1):1-4.

Answered by:
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2. Cholesterol-lowering agents and children

What is the youngest age at which cholesterol-lowering agents can be safely used?

Submitted by:
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Bile acid resins have been used for many years in children older than age 10 with familial hypercholesterolemia. It is difficult for children to use the granules and there is a risk of choking on the large cholestyramine tablets. Colestipol tablets are more palatable for this age group. The effect is a reduction in low-density lipoprotein (LDL) of 10% to 20%.

There have been five published clinical trials of statin therapy since 1996 (simvastatin, pravastatin, lovastatin and atorvastatin) in children older than age 10, but none are approved yet for use in this age group in Canada. Lowering cholesterol levels in childhood has not been shown to reduce coronary artery disease (CAD) in adult life. In fact, many children with hypercholesterolemia do not meet the criteria for treatment in adulthood.

It is important to be aware of the guidelines for screening only selected children at risk using non-fasting total cholesterol levels and to measure fasting lipids when the total cholesterol (TC) is > 5.2 mmol/L. It is imperative to work with a nutritional expert when working with children to maximize lifestyle intervention when LDL > 3.4 mmol/L. The guidelines for drug therapy when LDL > 4.9 mmol/L are based on a family history of hypercholesterolemia or LDL > 4.1 mmol/L with a family history of CAD before age 55. These levels are very different than the levels recommended for adults with risk factors, such as diabetes. See **www.aap.org** for guidelines.

Recommended reading
1. Belay B, Belamarich P, Racine AD: Pediatric Precursors of Adult Atherosclerosis. Pediatr Rev 2004; 25(1):4-14.
2. McCrindle B: Lipid abnormalities in Children with Metabolic Syndrome. Can J Diabetes 2004; 28(3):226-37.
3. American Academy of Pediatrics. Committee on Nutrition. Cholesterol in Childhood. Pediatrics 1998; 101:141-7.
4. Canadian Diabetes Association 2003 Clinical Practice Guidelines for the Prevention and Management of Diabetes in Canada. Type 2 diabetes in Children and Adolescents. Can J Diabetes 2003; 27:S91-93.

Answered by:
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3. What's the connection between peanut and tree nut allergies?

What is the connection between peanut and tree nut allergies?

Submitted by:
R. Braun, MD, CCFP
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These two food allergies share a propensity to cause life threatening anaphylactic reactions. This is due to the large size, complexity and stability of their protein structures, a property that distinguishes more potent allergens (nuts, peanuts, fish and crustaceans) from milk, eggs and other fruits and vegetables. These latter allergens are more easily broken down and become unrecognized when denatured by heat or enzymatic action.

Peanuts belong to the legume family. Thus, they are distinct antigenically from tree nuts and seeds. Notably, clinical cross reactivity between peanuts and other legumes, such as soy, peas, lentils and beans, is not significant. That is, we do not tell patients allergic to peanuts to avoid other legumes, unless there are other reasons to do so.

Patients with a nut allergy are often told to avoid other nuts because of potential cross reactivity, although little information exists to validate this belief (note that water chestnuts, coconut, and nutmeg are not tree nuts). Similarly, patients allergic to peanuts mistakenly avoid nuts as well. Although multiple asymptomatic sensitivity (skin test positivity) may be common, it is unlikely that a patient allergic to nuts will actually react to a variety of different nuts. However, until this patient is carefully addressed with blinded challenge studies, caution must be exercised in recommending the ingestion of different nuts in nut allergic patients.

It is important to note that an atopic patient will have an increased risk of reacting to food and environmental allergens in general, and thus the presence of a severe food allergy would make another allergy (food or environmental) more likely. Especially in children, we will frequently recommend the avoidance of all nuts in patients allergic to peanuts, due to the risk of cross-contamination; the foods that may contain peanut, may often contain nuts as well.

Answered by:
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4. Diabetic nephropathy and IHD: ACE or ARB?

Is it recommended to use an ACE inhibitor or an ARB as first-line treatment in a patient with diabetes with overt nephropathy and ischemic heart disease?

Submitted by:
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Answered by:
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Both angiotensin-converting enzyme (ACE) inhibitors and angiotensin receptor blockers (ARBs) are used extensively in the management of hypertension, particularly in patients with diabetes. In addition to the improvement in morbidity and mortality associated with the reduction of blood pressure, there is increasing evidence that some agents may provide important benefits beyond those that can be attributed to their antihypertensive effects. For instance, both ACE inhibitors and ARBs have been shown in numerous studies to reduce the progression of proteinurea in patients with diabetic nephropathy. In addition, the ARBs, losartan and irbesartan have been shown to delay the doubling of serum creatinine and reduce the development of end-stage renal disease. ARBs have also shown to be reasonable alternatives to ACE inhibitors in the management of patients with congestive heart failure. However, evidence favouring a true cardioprotective effect of ARBs is not as robust as that with ACE inhibitors.

Studies have demonstrated that patients with diabetes and other risk factors experience a significant reduction in myocardial infarction, stroke and death with the use of ramipril and perindopril, respectively. Thus, based on the currently available evidence, I would prefer to use an ACE inhibitor for a patient with diabetes, particularly if they have known ischemic heart disease or are at an increased risk (which, by having diabetes, they are) for it.

This is in accord with the 2003 Canadian Diabetes Association guidelines, which recommend the use of ACE inhibitors as first-line agents for vascular protection. However, some studies did not demonstrate a convincing advantage of using an ACE inhibitor over other antihypertensives. Thus, it needs to be emphasized that the bottom line should be reaching the target blood pressure (< 130/80 mmHg); how that target is reached is not more important than the need to achieve it.

Recommended reading
1. Siebenhofer A, Plank J, Horvath K, et al: Angiotensin receptor blockers as antihypertensive treatment for patients with diabetes mellitus: Meta analysis of controlled double-blind randomized trials. Diab Med 2004; 21(1):18-25.
2. Ball SG, White WB: Debate: Angiotensin converting enzyme inhibitors versus angiotensin receptor blockers: A gap in evidence-based medicine. Am J Cardiol 2003; 91(10A):15G-21G.
3. Kirpichnikov D, Sowers JR: Role of ACE inhibitors in treating hypertensive diabetic patients. Curr Diab Rep 2002; 2(3):251-7.
4. Rosner MH, Okusa MD: Combination therapy with angiotensin converting enzyme inhibitors and angiotensin receptor antagonists in the treatment of patients with Type 2 diabetes mellitus. Arch Intern Med 2003; 163(9):1025-9.

5. Bipolar disorder: Lithium or divalproex?

When treating bipolar disorder, what type of patient is better treated with lithium as a first-line agent over divalproex?

Submitted by:
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Lithium is a drug with beneficial effects on treating depression (weakest effect), treating mania, preventing depression and preventing mania. All of these effects have been validated with double-blind, placebo-controlled trials. Lithium has been demonstrated to also prevent suicide (in some studies by 700%) in comparison to other medications used for bipolar disorder. This effect may occur in other patients.

Valproate has been shown in double-blind, placebo-controlled trials to be an effective treatment of mania only. All other benefits of valproate seem to occur clinically, but have not been demonstrated scientifically to the rigor of the double-blind, placebo-controlled trials.

Both medications have potentially serious side-effects, but they are usually not worse than the illness. The drug that has given benefit to the patient should be tried first. The important thing is to prescribe either medication so that the patient can tolerate it.

From a side-effect perspective, people with liver disease should first be placed on lithium. People with kidney disease should be prescribed lamotrigine, olanzapine, quetiapine, risperidone, carbamazepine or valproate first. The evidence for effect is probably in that order. Many patients require a combination of medication and psychotherapy to obtain optimal results.

Answered by:
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6. Managing Osgoode Schlatters

How is Osgoode Schlatters managed?

Submitted by:
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Osgood Schlatters disease is a common cause of pain and tenderness of the tibial tuberosity in active adolescents. It is a self-limiting condition.

The patellar tendon inserts into the tibial tuberosity. During adolescence, there is a growth area called an apophysis. With excessive jumping or running activities, this area will have a significant amount of forces subjected to it, causing micro-avulsions of this area with subsequent attempts at repair. This will cause localized tenderness, swelling and minor impairment of knee function. X-rays are not required for diagnosis, but will occasionally show some fragmentation.

Osgood Schlatters occurs more often in boys than girls. Girls tend to have an earlier involvement between the ages of 11 and 13, whereas boys are between 12 and 15. Resolution is usually with completion of a growth spurt at age 14 for girls and age 16 for boys. The condition is bilateral 30% of the time. Complete resolution typically occurs within two years. A similar condition of the inferior pole of the patella can mimic it (Sinding–Larsen–Johansson Disease).

X-rays are not indicated, but if done, will show some fragmentation of the tibial apophysis.

Treatment includes activity modification, ice, protective padding, quadriceps and hamstring strengthening and acetaminophen or anti-inflammatory agents. The activity modification is avoidance of activities requiring significant quadriceps activity or contractions (*i.e.,* jumping, running). Immobilization and surgical treatment are rarely indicated.

The patient will be left with a prominence that may bother them later in life with kneeling activities and pre-dispose them to bursitis. Occasional surgical treatment is warranted, but rare.

Answered by:
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7. What's the incidence of edema with olanzapine?

What is the incidence of edema with olanzapine? I have seen a number of cases of upper and lower extremity and facial edema, which usually necessitates discontinuation of treatment.

Submitted by:
David Bloom, MD
Verdun, Québec

Premarketing trials of olanzapine reported an incidence of peripheral edema of up to 3%. Reports of edema with olanzepine are based on spontaneous reports and are likely underestimated; as such the true incidence is not known. It may be associated with older age and greater frequency of thyroid abnormalities. Little is known about the pathophysiology. If it were to occur, it's not known if dosing manipulation makes any difference. Some patients have used support stockings with some benefit. Fortunately, severe edema is rare.

Answered by:
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Memorable Quote

"A disease known is half cured."

Thomas Fuller

8. Stable CAD patients and clopidogrel

Should all patients with stable coronary artery disease be placed on clopidogrel?

Submitted by:
Anne MacCara, MD
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Certainly, all patients with coronary artery disease should be offered antiplatelet therapy. Acetylsalicylic acid (ASA), 81 mg, daily is the gold standard and should be offered to all persons with a 10-year coronary heart disease risk of 10% or more. Contraindications to ASA include impending or recent surgery, ASA sensitivity and a history of gastrointestinal bleeding.

Clopidogrel acts via a different mechanism and is an additive to ASA. In comparative studies, clopidogrel, either alone or added to ASA, is more effective than ASA alone. Both the relative and absolute benefits of clopidogrel are higher in high-risk individuals.

In the relatively low-risk cohort studied in Clopidogrel versus aspirin in Patients at Risk of Ischaemic Events (CAPRIE), 196 patients were treated with clopidogrel (instead of ASA) to prevent one cardiovascular event. On the other hand, in the Clopidogrel in Unstable angina to prevent Recurrent Events (CURE) trial, patients who had unstable angina or non-ST segment elevation myocardial infarction treated with stents, benefited for at least a year when clopidogrel was added to ASA. In these patients, the number needed to treat was 26. The recently published Management of ATherothrombosis with Clopidogrel in High-risk patients with recent transient ischemic attack or ischaemic stroke (MATCH) study prompts caution in using the combination.

In patients with a recent ischemic stroke or transient ischemic attack, ASA added to clopidogrel provided no more protection against ischemic events, but did increase the risk of life-threatening bleeding. Dx

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