Considerations for Testosterone Replacement Therapy

1.

A 60-year-old male on a testosterone supplement has elevated hematocrit and total cholesterol. Any concerns? How should he be managed?

Question submitted by:
Dr. Denis Cheung
Ottawa, Ontario

Testosterone replacement therapy generally does not negatively affect serum lipids (unlike abuse of anabolic steroids), so this is not a reason for dose/formulation adjustment.[1] Testosterone replacement therapy may increase hemoglobin/hematocrit and should not be started if the hematocrit is > 50%. Red cell mass may increase in a dose-dependent manner, more so in older men and in those with intramuscular testosterone esters. Men with obesity, sleep apnea, or COPD may be more susceptible. This may result from the effect of testosterone on erythropoietin, but recent data suggest testosterone may inhibit hepcidin, and, thus, regulate iron availability for erythropoiesis.[2] Because of concern for neurovascular events, testosterone needs to be withheld until the hematocrit falls below 50% and then reinstituted at half the dose while monitoring continues. Intramuscular formulations may be changed to oral or transdermal formulations.

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2. Bachman E, Feng R, Travison T, *et al*: Testosterone Suppresses Hepcidin in Men: A Potential Mechanism for Testosterone-induced Erythrocytosis. J Clin Endocrinol Metab 2010: 95(10):4743–4747.

Answered by:
Dr. Bernard Corenblum

Treatments for Sleep Apnea

2.

Besides continuous positive airway pressure (CPAP), are there any effective treatments for sleep apnea?

Question submitted by:
Dr. Sebouh Matossian
New Westminster,
British Columbia

There are causes other than upper airway obstruction for sleep apnea or, more correctly, sleep disordered breathing, and it is important to distinguish these before prescribing any intervention. Specifically, Cheyne-Stokes respiration (central sleep apnea) may be treated with adaptive servo-ventilation (ASV), and obesity hypoventilation syndrome (OHS) requires assisted ventilation with bilevel positive airway pressure (BiPAP). Continuous positive airway pressure (CPAP) remains the most effective treatment for uncomplicated obstructive sleep apnea (OSA).

Dental appliances to protrude the mandible are an alternative to CPAP. These are usually reserved for patients with mild to moderate OSA. They require adequate dentition and are limited by difficulty tolerating the device, alteration of the bite, and pain in the temporo-mandibular joints if protrusion is excessive. They are similarly priced to CPAP and about as effective in mild to moderate disease. Surgery to the palate, uvula, and pharynx has been popular as a potential fix for obstructive sleep apnea, but the data suggest that it is of low efficacy.

Tracheotomy has been used in the past and can be dramatically effective, but, in very obese subjects with short, fat necks with redundant folds, the tracheotomy can be obstructed. Furthermore, other risks and discomforts are associated with bypassing the protective upper airway and the vocal cords. As a result, tracheotomy has fallen out of favour.

Many individuals with OSA are obese, if not morbidly obese, and obesity is a risk factor for a wide range of other disorders. Realistically, the most efficacious method for treating obstructive sleep apnea in these individuals is to encourage them to lose weight. The poor response with many of the interventions for obesity has discouraged physicians from taking this route, but it is the one intervention that will have a comprehensive impact on health and quality of life. Additional lifestyle measures that may be helpful include avoidance of alcohol and sedatives close to bedtime and sleeping in the lateral position (in patients with supine-dependant OSA).

Answered by:
Dr. Robert Cowie and
Dr. Patrick Hanly

What to do about Low Hemoglobin and Low Ferritin Levels

3.

What do you do with a low hemoglobin and low ferritin levels? Is it necessary to prescribe iron supplements?

Question submitted by:
Dr. Sean Therrien
Hawkesbury, Ontario

Low hemoglobin (anemia) with low ferritin is defined as iron deficiency anemia, and patients typically present with a microcytosis (small red cells, as measured by mean corpuscular volumes).

However, other causes of anemia may also coexist and should be investigated if suspected. When a patient has an isolated, low ferritin level without anemia, this is called an iron-depleted state rather than iron deficiency anemia. In either case, the management or therapy is the same. It is essential to determine the underlying cause of iron deficiency, and it is necessary to replace the iron stores. Oral iron supplementation is the preferred initial route of supplementation. In patients who can not tolerate oral iron, are unable to absorb it, or have losses greater than expected, parenteral iron in the form of intravenous iron should be considered. We would advise clinicians to be cautious with iron replacement in older patients with hemoglobin in the high- to normal-range, as replacement may unmask an underlying polycythemia rubra vera.

Answered by:
Dr. Cyrus Hsia and
Dr. Kang Howson-Jan

Caffeine Consumption in Children

4.

Are caffeinated drinks, such as coffee and tea okay for children to drink in small quantities?

Question submitted by:
Dr. Steve Choi
Oakville, Ontario

Caffeinated drinks are fine to serve to children in small quantities. However, the amount of these beverages consumed by children must be very limited. The Health Canada Guidelines for caffeine intake recommend that children aged four- to six-years consume no more than 45 mg of caffeine per day, which is the amount found in approximately one cup of tea, one can of soda, or in one-third of a cup of coffee. If a parent is serving a child tea or coffee, the amount of caffeine the child is consuming from other sources, such as cola or chocolate, must also be taken into consideration so that the total daily dose of caffeine is not exceeded. Furthermore, most caffeine-containing beverages also have a very high sugar content, and, for that reason alone, their consumption should be limited. Caffeine is a stimulant that can have numerous negative effects on people, such as jitteriness or restlessness, difficulty sleeping, gastrointestinal upset, headaches, and difficulty concentrating. Children are especially prone to these effects, so their caffeine intake should be carefully monitored. So, as with all things, moderation is perhaps the best rule.

Answered by:
Dr. Krista Helleman

Steroids in Pregnancy

5.

How safe are steroids for asthma in pregnancy?

Question submitted by:
Dr. A. John B. Nazareth
Toronto, Ontario

Good asthma control to prevent hypoxia in mother and fetus is paramount during pregnancy. Steroids, for the most part, are safe in pregnancy, and they are an integral part of the management of asthma. Ideally, inhalational steroids are preferred to systemic or oral steroids given the theoretical risk of cleft lip and palate associated with systemic steroid use during the first trimester. This risk, identified in animal studies, has not been excluded in large-scale human cohort and case control studies, but the overall absolute risk quoted is an increase of 2 to 3 per 100,000 versus 1 per 100,000 background population risk. High doses of inhaled glucocorticoids may also cause congenital malformations in the first trimester, but the evidence is weak and inconclusive. There is good evidence that standard low to moderate doses of inhalational steroids are safe in pregnancy. Prednisone is preferred to other systemic steroids, as it does not cross the placental barrier. Systemic steroid use has been associated with preterm birth and low birth weight, as well as maternal diabetes and pre-eclampsia, but, on the balance, if required for severe asthma control, it can prevent more catastrophic outcomes.

Resource
1. Oren D, Nulman I, Makhija M, *et al:* Using Corticosteroids During Pregnancy: Are Topical, Inhaled, or Systemic Agents Associated with Risk? www.motherisk.org/women/updatesDetail.jsp?content_id=693. Accessed: June 19, 2013.

Answered by:
Dr. Cathy Popadiuk

Applying Results of the JUPITER Trial to Younger Patient Groups

6.

Are the results from the JUPITER Trial showing the risk-stratification utility of hs-CRP applicable in younger patient groups, as well?

Question submitted by:
Anonymous

The JUPITER Trial demonstrated the additional benefit of using the biomarker high-sensitivity C-reactive protein (hs-CRP) to better determine a patient's CV risk. Specifically, the trial showed that in apparently healthy persons without hyperlipidemia (LDL cholesterol < 3.5 mmol/L) but with elevated hs-CRP of greater than 2 mg/dl, rosuvastatin significantly reduced the incidence of major CV events. However, it must be noted that only men 50-years-of-age or older and women 60-years-of-age or older were eligible to take part in this trial. The Canadian guidelines, therefore, recommend reserving hs-CRP for patients in this age category who are at moderate risk for CVD with a Framingham Risk Score (FRS) between 10 to 20%, who have an LDL-C below 3.5 mmol/L, and are free of acute illness. Important risk modifiers for younger patients include a positive family history and the presence of the metabolic syndrome, either of which can double the FRS and help make a case for using statin therapy to reduce CV risk.

Answered by:
Dr. Theodore K. Fenske

When Should the Chicken Pox Vaccine Be Administered?

7.

If there is no known previous history of chicken pox, should we check titres or administer the vaccine? Up to what age should this be done?

Question submitted by:
Dr. Nathalie Leroux
Fenwick, Ontario

The vaccine is safe and free in most jurisdictions. Thus, for any children without a history of chicken pox, it is reasonable to give the vaccine without the bother and cost of titres. On the other hand, the great majority of adults who grew up in the prevaccine era are immune, whether or not they recall clinical varicella. It is probably not worth doing titres or vaccinating these adults.

There are currently no guidelines as to what the "magic" age limit is for presumed immunity, but there is now a sizable cohort of younger adults who may never have been exposed to natural disease. It has been suggested that anyone born after 1980, who does not have evidence of prior infection or vaccination, simply be vaccinated. For those born after 1980, immunity can be presumed to be present. An exception should be made for immigrants from tropical countries who are generally much less likely to be immune than Canadian-born adults. They should probably have titres done and be vaccinated as needed. Health care workers with no history of infection should also be tested and vaccinated as needed in order to protect their patients.

Answered by:
Dr. Michael Libman

Treating Elevated Triglycerides in an Otherwise Healthy Patient

8.

What drug would you use to treat elevated triglycerides in a patient with normal blood sugar and normal HDL/LDL cholesterol?

Question submitted by:
Dr. Maha Dutil
Toronto, Ontario

Elevated plasma triglyceride concentration is a common finding, but the evidence for the benefit of treating it is less extensive than that for treating elevated LDL cholesterol. It is frequently found in association with low HDL cholesterol, metabolic syndrome, obesity, and diabetes.

Hypertriglyceridemia increases the risk of acute pancreatitis, and, although some patients can develop pancreatitis when their fasting triglyceride concentration is 5 to 10 mmol/L, the risk becomes clinically significant when fasting measurements exceed 10 mmol/L.

Initially, patients with hypertriglyceridemia should be counselled about therapeutic lifestyle changes (*e.g.*, healthy diet, regular exercise, reducing alcohol intake, tobacco use cessation). Patients should also be screened for metabolic syndrome and other acquired or secondary causes (nephrotic syndrome, diabetes, chronic renal failure, hypothyroidism, various medications).

Optimizing glycemic control may improve hypertriglyceridemia. Statins, fibrates, niacin, and fish oil (alone or in various combinations) are effective when pharmacotherapy is indicated.

Resources

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2. Oh R, Lanier J: Management of Hypertriglyceridemia. American Family Physician 2007; 75(1365):1371–1372.

Answered by:
Dr. Brett Heilbron

9. Etiology of Osteomyelitis of the Spine or Discitis

Could you discuss the etiology with respect to osteomyelitis of the spine or discitis?

Question submitted by:
Dr. T. Cuddy, Burlington, Ontario

Vertebral osteomyelitis is often a difficult diagnosis. Other than post-operative infections, it is thought that most cases are due to hematogenous spread, often from an occult focus. Symptoms typically include localized, insidious pain and tenderness, which may easily be confused with mechanical pain, especially in the lower back. Fever may be absent, and even the peripheral leukocyte count may be normal. Therefore, a high index of suspicion is required. Investigation is difficult, as only MRI provides sufficient sensitivity to rule out the diagnosis. MRI often shows small paravertebral abscesses, which are not visible on CT. Nuclear scans may be suggestive, but the anatomic detail is poor. Even a CT-guided biopsy may miss the focus of infection. The infection usually starts in the intervertebral disc space via the segmental arterial supply. In the case of early discitis, it may be difficult to sort out infection from non-infectious inflammation of the disk. Sometimes, even in the absence of fever, the only clue may be a positive blood culture for a typical pathogen, such as *Staphylococcus aureus*. In summary, this is a difficult diagnosis, and spinal pain that is unusual or atypical, and does not respond to the usual treatments, should arouse suspicion.

Answered by:
Dr. Michael Libman

Dosage of Duloxetine for Depression

10. What is the recommended dosage of duloxetine for depression?

Question submitted by:
Dr. Gaetan Lavoie
Ste-Félicité, Québec

Duloxetine is a serotonin-norepinephrine reuptake inhibitor (SNRI). As such, it falls under the same class of medications as venlafaxine and desvenlafaxine. Duloxetine is not statistically different when dosed at 60 mg or 120 mg for major depressive disorder.[1-2]

However, duloxetine has certain multiaxial benefits. It is indicated for the treatment of neuropathic pain, though this benefit is dose-dependent. It is also indicated for anxiety. Higher doses have been demonstrated to be more beneficial than the "standard" depression dose of 60 mg per day. This is where assessment of the patient from a psycho-social angle comes into play.

For example, a patient with depression on Axis I and anxiety on Axis II, or neuropathic pain or fibromyalgia on Axis III, may benefit from doses in the range of 90 to 120 mg per day. Psychosocial issues, such as smoking, are also a factor. Smoking is a very potent inducer of cytochrome P450 1A2, of which duloxetine is a substrate. Patients who smoke at least seven cigarettes per day and take duloxetine may need higher doses of duloxetine by up to 50% to offset the effects of the polycyclic aromatic hydrocarbons from cigarette smoke just to control their depression. This may result in failure of therapy and the need for the physician to use higher doses to achieve the desired therapeutic effect.

Smoking cessation may increase the levels back to supratherapeutic dosing. For example, a patient with pain and depression may receive a dose of 120 mg per day, but their body is only systemically receiving 90 mg due to enzyme induction. Smoking cessation will then result in possible adverse effects, including blood pressure changes, irritability, and possible activation.

References
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2. Lamoure J, Stovel J: Are Duloxetine's Side Effects Dose Related? Medscape Pharmacist ATE December 2007. http://www.medscape.com/viewarticle/566867. Accessed: May 17, 2013.

Answered by:
Dr. Joel Lamoure

Any Treatments for the Prevention of Alzheimer's Disease?

11.

Have any recent studies been done for the prevention of Alzheimer's disease? Can any suggestions be made to persons with multiple family members affected?

Question submitted by:
Dr. D'Souza
North York, Ontario

There have been no successful prophylactic treatment options for Alzheimer's disease. If there are multiple family members affected, assessment by a geneticist could be considered.

Answered by:
Dr. Sarah A. Morrow

Medical Therapy vs. Intervention for Coronary Artery Disease

12. What are the criteria for treating patients with medical therapy versus intervention for coronary artery disease?

Question submitted by:
Dr. B.L. Chandarajan
Kingston, Ontario

The primary goals of both medical therapy and intervention for coronary artery disease include the reduction of symptoms (especially angina) and adverse events (including myocardial infarction, hospitalization with angina, and death). Typical anti-anginal therapies include nitrates, β-blockers, and calcium channel blockers. Vascular protection is achieved with ASA, a statin, and/or an ACE-inhibitor.

While early intervention, with the goal of revascularization through stenting or bypass of the occluded artery, is the preferred therapy for many patients with acute myocardial infarction, revascularization does not offer the same benefits for low- or intermediate-risk patients with stable coronary artery disease. The Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial provided the first high-quality evidence supporting the use of optimal medical therapy (OMT) in stable angina.[1] Over 2,000 patients with stable angina and high-grade stenosis of at least one coronary artery were randomized to OMT alone versus OMT with percutaneous coronary intervention (PCI) and were followed for nearly five years. Roughly equivalent proportions of patients had Canadian Cardiovascular Society grade one, two, or three angina, as well as single-, double-, or triple-vessel disease. Although, at one and three years of follow-up, more patients treated with PCI were angina-free, there was no difference in angina between the two groups at five years of follow-up. While PCI use reduced anginal symptoms and need for revascularization, it had no effect on the outcome of death and myocardial infarction, which supports the use of OMT alone for patients with stable angina.

The BARI 2D Bypass Angioplasty Revascularization Investigation 2 Diabetes (BARI 2D) trial was a trial of similar size, patient population, and design to COURAGE, with the only difference being that all enrolled patients had type 2 diabetes mellitus.[2] Again, after five years of follow-up, there was no difference in terms of death or major CV event between patients treated with PCI, or bypass surgery, versus OMT. A comprehensive meta-analysis found that when the data from 61 trials and over 25,000 patients was taken together, there was no difference in the rates of death or myocardial infarction in patients with stable angina treated with PCI versus OMT.[3]

With the understanding that PCI does not affect mortality rates in stable angina, it may be considered on a case-by-case basis for improvement of angina in patients who remain symptomatic despite OMT. Patients with refractory symptoms or high-risk features on noninvasive testing, (such as extensive ischemia on exercise treadmill testing, myocardial perfusion imaging, stress echocardiography, or stress magnetic resonance imaging) require invasive cardiac catheterization in order to determine their suitability for revascularization, either by PCI or coronary artery bypass grafting.

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Answered by:

Dr. Richard Vandegriend
Dr. Brett Heilbron

Breast-conserving Surgery vs. Mastectomy

13.

Why are most surgeons recommending breast-conserving surgery as opposed to mastectomy when recurrence rates are higher with breast-conserving therapy?

Question submitted by:
Dr. Nirvashni Rughubir
Mississauga, Ontario

Essentially, the bottom line is that there are no survival differences between breast conserving surgery (BCS; lumpectomy), plus whole breast radiotherapy compared with mastectomy in patients with early stage breast cancer.[1-2] Certainly, BCS is more pleasing from a cosmetic and psychological standpoint, and it is often a patient preference. Nonetheless, there are a number of factors that need to be taken into account when deciding on BCS versus mastectomy including tumour size and location, ability to achieve negative surgical margins, other needs or contraindications for radiotherapy, and the presence of extensive ductal carcinoma in situ.

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Answered by:
Dr. Roger Y. Tsang

Is It Possible for an Asthmatic Patient to Have Normal PFTs?

14.

Is it possible to have asthma but normal PFTs (pulmonary function tests)?

Question submitted by:
Dr. Danielle Fish
Canton de Hatley, Québec

Spirometry, the measurement of forced vital capacity (FVC), forced expiratory volume in one second (FEV1), and the ratio of FEV1 to FVC, may often be normal in patients with mild asthma. Even when the initial tests are normal, there might be a significant improvement when the test is repeated after giving inhaled salbutamol — a finding that would suggest the diagnosis of asthma. In patients with mild (especially mild, intermittent asthma), both the pre- and post-bronchodilator measurements may be normal. However, it would be very unusual for a patient with current symptoms suggesting asthma to have normal spirometry. That confluence would suggest that the diagnosis of asthma is erroneous. It is important to realize that asthma-like symptoms are common, and, when they occur in association with normal lung function, the diagnosis of asthma is usually wrong.

A diagnosis of asthma can be ruled out by a normal result from a methacholine challenge test. It is usually done in patients with asthma-like symptoms and normal spirometry. Such a finding would allow the patient to stop using expensive asthma medication and the physician to concentrate on the management of "pseudo-asthma."

Answered by:
Dr. Robert Cowie

Treating Acute CHF with Relaxin

15.

Is relaxin useful for treating acute congestive heart failure (CHF)?

Question submitted by:
Dr. Edwin J. Franczak
Toronto, Ontario

Relaxin is a naturally occurring human peptide that was initially considered a reproductive hormone, since it functions to both enhance sperm motility and to facilitate labour by the softening of the pubic symphysis. More recently, other biologic properties of relaxin have been demonstrated, including anti-inflammatory, extracellular matrix remodelling, angiogenic, and anti-ischemic effects, creating interest for its utility in modulating CVD. Data from the pre-Relaxin for the Treatment of Acute Heart Failure (RELAX-AHF) trial have demonstrated that relaxin may have a potential role in the treatment of acute heart failure. However, these are early days. While relaxin looks promising, it is currently under research and is not available for the management of heart failure patients.

Answered by:
Dr. Theodore K. Fenske

Treating Anemia in Children

16.

How does one treat anemia (iron deficiency) in children?

Question submitted by:
Dr. Silvia Vignado
Winnepeg, Manitoba

There are four main components to successfully treating iron deficiency in children. First, it is important to ensure that you are actually treating anemia that is due to a deficiency of iron and not to some other blood disorder, such as lead poisoning or thalassemia.

Oral iron therapy is still the mainstay of treatment. Children with iron deficiency need to receive 3 to 6 mg/kg of elemental iron per day, usually in the form of ferrous sulfate. The amount of iron needed will depend on the severity of the anemia and can be given once or twice a day. The maximum daily dose should not exceed 150 mg of elemental iron. Iron is best absorbed when it is given between meals and with juice, instead of milk or formula.

The child's diet also needs to be modified. Cow's milk intake should be limited to less than 20 oz per day. The child should also be encouraged to eat more iron-rich foods, such as meat, fish, eggs, iron-fortified cereal, legumes, and green vegetables.

Finally, follow-up testing needs to be done to ensure a response to therapy. Hemoglobin should be rechecked in four weeks. Adequate therapy should produce a hemoglobin rise of greater than 10 g/L. The CBC should then be re-evaluated every two to three months until the hemoglobin normalizes. Iron therapy should be continued for two to three more months after normal hemoglobin is reached in order to replace iron stores.

Answered by:
Dr. Alexander K.C. Leung

Blood Pressure Variations between Arms

17.

When patients have wide blood pressure variations between arms, which reading (higher or lower) should be considered accurate?

Question submitted by:
Dr. Lynda Nguyen
Edmonton, Alberta

Your question is a good one, because it raises an important point about taking blood pressure. The quick answer is that the higher number is always correct. Disease in the arteries will only result in lowering blood pressure. There is no real mechanism to significantly increase blood pressure in one arm above that generated by the heart.

As you know, the difference in blood pressure between arms can be seen fairly often in general populations, including healthy women during the antenatal period. Clinical guidelines for hypertension consider an interarm difference of less than 10 mmHg to be normal. Differences greater than 20 mmHg indicate underlying vascular disease. A recent study has shown that differences of this magnitude can predict an increased risk of CV events and all-cause mortality over 10 years. The presence of interarm differences is one of the explanations for a delayed diagnosis of hypertension and is also related to poor control of hypertension. Choosing the lower blood pressure arm as the correct reading can mislead you with regards to the course of treatment. It is suggested that taking blood pressure in both arms, especially at the first visit with a new patient, should be a standard of practice.

Answered by:
Dr. Wayne Warnica

Adenomyomatosis and Follow-up Treatment

18.

What follow-up is required for the diagnosis of adenomyomatosis found on an ultra sound of the gallbladder?

Question submitted by:
Dr. Micahel Cain
Ottawa, Ontario

Gallbladder adenomyomatosis is a disease characterized by proliferation of the mucosal epithelium and hypertrophy of the muscularis mucosae, resulting in mucosal invagination within the thickened muscularis layer and radiologically-identifiable intramural diverticula or invaginations (called Rokitansky-Aschoff sinuses).[1] Most patients with gallbladder adenomyomatosis are asymptomatic; this condition typically presents as an incidental finding on imaging or histological examination of surgical gallbladder specimens, although it can occasionally present with right, upper-quadrant abdominal pain with or without the presence of cholelithiasis.[2] Adenomyomatosis (particularly segmental presentations) may be associated with an elevated risk of gallbladder malignancy, although there is a paucity of definitive evidence in this regard.[3-5] Follow-up for gallbladder adenomyomatosis is typically not required unless there are associated symptoms or atypical features that are concerning for evolving or overt malignancy. Patients presenting with symptomatic adenomyomatosis or lesions suggestive of adenomyomatosis that are indistinguishable from pre-malignant or malignant disease, are considered as an indication for cholecystectomy.[1,2]

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Answered by:
Dr. Theodore Xenodemetropoulos

Testing Diabetics for Silent Ischemia

19. Should all diabetics who have noninsulin-dependent diabetes mellitus (NIDDM) be tested for silent ischemia? If yes, when?

Question submitted by:
Dr. Renu Bajaj
Waterloo, Ontario

Although it's rather disconcerting to the practicing clinician who is trained to respond to patient complaints, myocardial ischemia can occur without overt symptoms. In fact, it's been shown that asymptomatic ST-segment depression during ambulatory EKG monitoring occurs more often than symptomatic ST-segment depression in patients with coronary artery disease.[1] Due to autonomic nervous system assault, silent ischemia is more common in patients with type 1 and 2 diabetes than in the general population, especially in men over 60-years-of-age with microalbuminuria.[2] As such, noninvasive exercise stress testing plays an important role in identifying diabetic patients with silent ischemia, and it should be considered to detect asymptomatic coronary artery disease. Since noncardiac surgery is associated with an increased risk of CV morbidity and mortality, preoperative CV risk assessment is recommended for diabetic patients.[3] As well, routine screening of patients with NIDDM would be prudent for those in whom the duration of diabetes exceeds 10 years, particularly if other CV risk factors are present.[4]

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Answered by:
Dr. Theodore K. Fenske

Survival Rate of a Patient Treated for Pancreatic Cancer

20.

What is the actual survival rate (in months) of a patient with pancreatic cancer who is treated?

Question submitted by:
Dr. Michel Pineau
Rimouski, Québec

For metastatic pancreatic cancer, the median overall survival (OS) rate is six to seven months with single-agent gemcitabine chemotherapy, a standard first-line treatment option for patients who are candidates for chemotherapy. Recently, the combination regimen FOLFIRINOX (5-fluorouracil, leucovorin, irinotecan, oxaliplatin) was evaluated in the ACCORD 11 trial and reported a median OS of 11.1 months.[1] This Phase III trial randomized 342 patients with chemotherapy-naive, metastatic pancreatic cancer to receive intravenous chemotherapy with FOLFIRINOX or gemcitabine. Inclusion criteria included a good performance status (Eastern Cooperative Oncology Group performance status score of 0 or 1) and a serum bilirubin of less than 1.5 times the upper limit of normal. The primary endpoint of OS was met at the time of a preplanned interim analysis after 250 patients were enrolled, with a median OS of 11.1 months in patients receiving FOLFIRINOX versus 6.8 months in patients receiving gemcitabine. Additionally, the objective response rate was higher with FOLFIRINOX (31.6% versus 9.4% with gemcitabine), as was the progression-free survival rate of 6.4 versus 3.3 months. However, greater treatment-related toxicities were seen with the FOLFIRINOX regimen, including cytopenias, febrile neutropenia, sensory neuropathy, GI toxicity (*e.g.,* vomiting, diarrhea), and fatigue.

Reference
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Answered by:
Dr. Roger Y. Tsang

Protecting Children against Insect Bites

21.

What measures do you recommend to protect a child, newborn to two-years-of-age, from insect bites?

Question submitted by:
Dr. Danaze Chambers
Banff, Alberta

Insect repellents containing DEET are the most common and effective products for protecting individuals from insect bites. The Health Canada Guidelines state that it is safe to use products containing up to 10% DEET, applied once daily, in children aged six-months to two-years. This single DEET application will provide protection from insect bites for a three-hour period. It is important to avoid the mouth and eyes when applying these products and to keep the child's hands free of the chemical, as children often put their hands in their mouths. However, DEET-containing products are not safe for use in children under six-months-of-age. In this age group, alternative protection must be used. Products containing 2% soybean oil are effective and safe for all age groups but are not widely available. Consequently, nonchemical methods are the best way to protect all young children from insect bites. These methods include the use of mosquito netting over strollers and cribs, staying inside during dusk and dawn when mosquitoes are most active, and wearing light-coloured clothing, preferably with long sleeves and pants, when in areas where insects are ubiquitous.

Answered by:
Dr. Krista Helleman

Loss of Libido in an Otherwise Healthy Woman

22.

Are there any evidence-based treatments for the loss of libido in an otherwise healthy women?

Question submitted by:
Dr. Nicki Wilberforce, Rosslyn, Ontario

Libido refers to a person's sexual desire — the first phase of the sexual act that is comprised of desire, arousal, orgasm, and resolution. Loss of libido is also referred to as hypoactive sexual desire disorder (HSDD). Several factors can affect libido: biological, psychological, relationship, and social-cultural. Before attempting any therapeutic agents for loss of libido in an otherwise healthy woman, relationship, psychological, and social factors should be addressed, and the etiology for the impaired libido should be identified.

For residual biological problems, a number of studies have looked at various hormonal therapies and other medications. There is good evidence that supplemental androgen therapy, orally and transdermally, is effective when added to systemic HRT — estrogen and progesterone for uterine protection — in postmenopausal women with low libido, but there are few studies of testosterone treatment alone that were completed after the negative concerns for HRT were identified. The limited data, however, suggests the beneficial effect of testosterone patches alone in postmenopausal women. There is also data to suggest that testosterone may help premenopausal women's HSDD, but the evidence is limited to small trials with scant safety data. Caution must be used with androgen therapies due to potential masculinizing side effects. Phosphodiesterase inhibitors (*e.g.,* sidenafil) for low libido in healthy women have not been shown to be efficacious in randomized trials, although there may be some benefit in women taking SSRIs. None of these agents are approved in North America to treat libido in otherwise healthy women. Consideration for their use requires a thorough discussion regarding risks and benefits in a well-informed patient.

Resource
1. Lamont J: Female Sexual Health Consensus Clinical Guidelines. J Obstet Gynaecol Can 2012; 34(8):769–775.

Answered by:
Dr. Cathy Popadiuk

Liraglutide for Nondiabetic, Obese Patients

23.

At what dosage can liraglutide be administered to control obesity in nondiabetic patients?

Question submitted by:
Dr. Stan Van Duyse
Montréal, Québec

Please note that liraglutide is not currently approved for the treatment of obesity in nondiabetic individuals. However, liraglutide is currently being investigated as a potential agent for weight management in obese or overweight patients with or without type 2 diabetes. In one randomized, double-blind placebo-controlled trial, liraglutide at 1.2, 1.8, 2.4, or 3 mg was more effective than both a placebo and orlistat in causing weight loss in obese individuals without type 2 diabetes. The mean weight loss for liraglutide 1.2 mg was 4.8 kg compared to 7.2 kg weight loss achieved with 3 mg of liraglutide. About 52% of patients lost more than 5% of their baseline weight at 20 weeks on 1.2 mg liraglutide compared to 76% on 3 mg liraglutide. 7.4% of patients lost more than 10% of their baseline body weight on 1.2 mg of liraglutide compared to 28% on 3 mg of liraglutide. As expected, adverse effects were seen more frequently in the high dose liraglutide group, with 71% of patients in the 3 mg group reporting some gastrointestinal side effects compared to 53% on 1.2 mg and 30% on a placebo. A two-year extension of this trial demonstrated that the weight loss is sustained over a period of two years, and it was associated with an improvement in CV risk factors, such as a reduction in the prevalence of prediabetes and metabolic syndrome. It is also associated with improvements in blood pressure and lipid profile.

Resource
1. Astrup A, Rössner S, Van Gaal L, *et al*: Effects of Liraglutide in the Treatment of Obesity: a Randomised, Double-blind, Placebo-controlled Study. Lancet 2009; 374(9701):1606–1616

Answered by:
Dr. Hasnain Khandwala

When Should the Chicken Pox Vaccine Be Administered?

24.

If there is no known previous history of chicken pox, should we check titres or administer the vaccine? Up to what age should this be done?

Question submitted by:
Dr. Nathalie Leroux
Fenwick, Ontario

The vaccine is safe and free in most jurisdictions. Thus, for any children without a history of chicken pox, it is reasonable to give the vaccine without the bother and cost of titres. On the other hand, the great majority of adults who grew up in the prevaccine era are immune, whether or not they recall clinical varicella. It is probably not worth doing titres or vaccinating these adults.

There are currently no guidelines as to what the "magic" age limit is for presumed immunity, but there is now a sizable cohort of younger adults who may never have been exposed to natural disease. It has been suggested that anyone born after 1980, who does not have evidence of prior infection or vaccination, simply be vaccinated. For those born after 1980, immunity can be presumed to be present. An exception should be made for immigrants from tropical countries who are generally much less likely to be immune than Canadian-born adults. They should probably have titres done and be vaccinated as needed. Health care workers with no history of infection should also be tested and vaccinated as needed in order to protect their patients.

Answered by:
Dr. Michael Libman

Erythromelalgia Treatment

25.

Are there any good new treatments for erythromelalgia?

Question submitted by:
Dr. C. Lynde
Markham, Ontario

This remains a very frustrating condition to treat. ASA, NSAIDs, and opiate pain control remain the main tools we have. On the horizon, a better understanding of the mechanisms causing this vascular instability may pave the way for pharmaceutical developments. For instance, the studies revealing a role for sodium channel Na(V)1.7 mechanisms in this disease offer hope for new avenues of research. An agent under study (XEN402) which inhibits the SCN9A sodium channel is showing promise for nonopiod approach to treat the severe pain associated with this disorder.

Answered by:
Dr. Scott Murray

Different Uses for Atomoxetine

26.

Is atomoxetine an antidepressant or antianxiety drug?

Question submitted by:
Anonymous

Atomoxetine is a norepinephrine reuptake inhibitor (NRI) medication. The medication was initially created as a unique agent to help control the impulsivity component of adult attention deficit disorder (ADHD). The rationale for this may lie in the fact that the gold standard of therapy for ADHD is the stimulant class of medications, which enhance dopamine. Dopamine, in turn, is converted in the body by dopamine-β-hydroxylase to norepinephrine.

Atomoxetine has found support as an adjunct in Alzheimer's (similar to methylphenidate). With respect to depression or anxiety, there is not a solid indication for atomoxetine's use. However, it may be considered as an adjunct for therapy. More interesting, a use for atomoxetine that does interface depression and anxiety is its use in post-traumatic stress disorder, which is an imbalance of several neurotransmitters including norepinephrine, serotonin, and dopamine. This is an emerging area, and atomoxetine may be considered as an adjunct for this patient population, starting at a dose of 25 mg per day and titrating up to a maximum of 100 mg per day.

Concerns with atomoxetine include CV side effects and potential interactions with inhibitors (or poor metabolizers) of cytochrome P450 2D6, such as paroxetine or fluoxetine, plus the "black box" warning of increased suicidality in teens and young adults.

Answered by:
Dr. Joel Lamoure

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