Consultant's Corner

Practical Answers To Your Everyday Questions

1. How Common is Serious Metformin-related Lactic Acidosis?

How common is serious metformin-related lactic acidosis, and should we be using it in cardiac patients?

Question submitted by:
Dr. M. Gagliardi
Sidney, British Columbia

Metformin is an effective first line oral hypoglycemic agent used since the 1950s (available in Canada since 1980) in the treatment of type 2 diabetes mellitus for its insulin-sensitizing benefit. When taken as directed, metformin is effective, inexpensive, and safe, standing alone as the only oral hypoglycemic agent with trial data demonstrating reduced mortality.

The UK Prospective Diabetes Study (UKPDS) showed a substantial beneficial effect of metformin therapy on CVD outcomes, with a 36% relative risk reduction in all cause mortality and a 39% relative risk reduction in myocardial infarction.[1] While there may be a theoretical risk of lactic acidosis when metformin is used in the context of contrast dye exposure from renal stress, such as following cardiac catheterization, this risk is exceedingly rare and should not deter physicians from making use of this important agent. There is no evidence from prospective comparative trials or from observational cohort studies that metformin is associated with an increased risk of lactic acidosis or with increased levels of lactate compared to other antihyperglycemic treatments.[2] Nonetheless, it remains common practice to avoid metformin 48 hours before coronary angiography. Until a randomized clinical trial can establish the precise incidence of metformin-induced lactic acidosis in this setting, this seems like a prudent precaution.

References
1. UK Prospective Diabetes Study Group: A Randomized Trial of Efficacy of Early Addition of Metformin in Sulfonylurea-treated Type 2 Diabetes (UKPDS 28). Diabetes Care 1998; 21(1):87–92.
2. Salpeter S, Greyber E, Pasternak G, *et al*: Risk of Fatal and Nonfatal Lactic Acidosis with Metformin Use in Type 2 Diabetes Mellitus. Cochrane Database Syst Rev 2003;(2):CD002967.

Answered by:
Dr. Theodore K. Fenske

Treating Pruritus Ani

2.

How can you best treat pruritus ani?

Question submitted by:
Dr. George Poland
Pierrefonds, Québec

A careful history and physical examination is the essential first step. There are many causes for pruritus ani, including parasite infestation, psoriasis, atopic dermatitis, Crohn's disease, hemorrhoids, neurodermatitis, allergic contact dermatitis, and fecal incontinence. A clear diagnosis can lead to a treatable primary cause. A common cause of anal itching is irritation from soiling and sometimes overzealous cleansing of the area. Restoration of good bowel routines with adequate fibre and oral fluid intake can reduce irritation from soiling, or exacerbation from hemorrhoidal itching. The use of mild nonfragrance cleansers and moisturizers, preferably with an ointment base, can be very soothing, especially after bowel movements.

Answered by:
Dr. Scott Murray

Autism and Vaccines

3.

Is there a link between autism and vaccines?

Question submitted by:
Dr. Jorge Burneo
London, Ontario

There is much smoke — and little fire — with respect to this question. It has been fueled by media attention and celebrities who make bold claims as to the connection between autism and vaccines in the absence of evidence linking the two. While it appears unquestionably true that there has been an increase in the number of children diagnosed with autism spectrum disorder (ASD) over the past several decades, a number of studies have failed to demonstrate a causal relationship between vaccines and the disorder. The American Academy of Pediatrics and the Canadian Paediatric Society have both issued statements claiming that there is no link between vaccines and autism spectrum disorder, and a 2008 case-control study supports this.[1]

This is an important question, as inadequate immunization of the siblings of children with autism spectrum disorder places them at risk; notably, over the past several years there have been outbreaks of both rubella and measles, both vaccine-preventable disorders. As well, a fixation on the association between vaccines and autism spectrum disorder — which probably does not exist — distracts time and resources from studying the actual reason(s) for the increasing number of diagnoses of ASD.

Reference
1. Hornig M, Briese T, Buie T, *et al*: Lack of Association Between Measles Virus Vaccine and Autism with Enteropathy: A Case-control Study. PLos ONE 2008; 3(9):e3140.

Answered by:
Dr. Michael Rieder

Treatment for Cramps

4.

Are there any proven treatments for cramps?

Question submitted by:
Dr. Andre Lalonde
Laval, Québec

Menstrual cramps, or primary dysmenorrhea (PD), is a common condition in women associated with their menstrual cycles. Ovulatory cycles create a surge in progesterone resulting in a cascade of prostaglandin (PG) changes, which can cause severe uterine muscle cramps. Secondary dysmenorrhea (SD) refers to menstrual cramps due to other gynecologic causes, such as endometriosis, endometrial or cervical polyps, pelvic infections, or other such conditions. SD should be considered in a woman who has developed menstrual cramps with no history of painful periods. The treatment for SD must address the cause; hence, efficacy will depend on the treatment options available for the particular diagnosis. Effective treatments for PD include NSAIDs, which inhibit PGs, and/or the oral contraceptive pill (OCP), which prevents ovulation. If symptoms do not improve with NSAIDs or OCPs, and if other gynecological causes for the menstrual cramps have been excluded, other less proven treatments can be explored. There is limited evidence that high-frequency transcutaneous electrical nerve stimulation (TENS), acupuncture, or topical heat may be helpful as well as Vitamin B1. Several other vitamins and minerals have shown some initial promising results, but further study is required. These include vitamin E, B6, B12, magnesium, and fish and other oils. If conservative therapies are ineffective and the PD significantly impacts on quality of life, surgery to remove the gynecologic structures is a final resort.

Answered by:
Dr. Cathy Popadiuk

Event Monitors (Recorders) vs. Holter Monitors

5.

What is the difference between an event monitor and a Holter monitor?

Question submitted by:
Dr. Glora Huang
Vancouver, British Columbia

Holter monitors and event monitors (recorders) are both types of ambulatory recording devices. They are primarily used to detect cardiac arrhythmias that were not detected by a standard electrocardiogram. Examples of such use, include the assessment of palpitations and checking for arrhythmias that may cause syncope.

For both monitors, the patient is attached to the device by electrocardiographic wires, similar to a standard electrocardiogram, but, in this case, only three leads are used. The Holter monitor will record a continuous electrocardiographic rhythm strip over 24 to 48 hours. The duration of recording is prolonged when the symptoms occur less frequently. The analyst will then have recordings of every heart beat and any rhythm disturbances over that period of time.

The event monitor is used for events or symptoms that are perceived to occur infrequently, or at unpredictable times, over multiple days. The recorder is a kind of "continuous loop recorder"; therefore, when the subject perceives he or she is having symptoms of interest, the record button is pressed. The device then records and freezes all the electrocardiographic activities for 30 seconds prior to the button being pressed, capturing the all-important onset of any rhythm abnormalities.

A newer type of event monitor is a small implantable device that is usually inserted under the skin of the patient's chest. This device is a "continuous loop recorder" that only saves electrocardiographic rhythm strips after the telemetry button carried by the patient is activated. It may store up to 40 minutes of activity after the button is pressed. The advantage of this type of device is that it can be used over 30 to 60 days while recording multiple events or taken out after the event in question has been clearly recorded.

Answered by:
Dr. Wayne Warnica

What Are the Best Iron Supplements to Prescribe?

6.

Is one iron supplement better than another?

Question submitted by:
Dr. Charles Lynde
Markham, Ontario

The most commonly prescribed types of ferrous iron supplements can be differentiated with respect to their elemental iron concentration. These include ferrous sulfate (20%), ferrous gluconate (12%) and ferrous fumarate (33%).[1] There is little evidence to suggest significant differences in bioavailability amongst the various types of oral iron supplementation.[1] Some data has indicated that sustained-release iron formulations may result in decreased nausea and epigastric pain in comparison to conventional ferrous sulfate, although therapy adherence rates between these formulations have been found to be similar.[2] Furthermore, enteric-coated and sustained release formulations are not as well absorbed as the nonenteric-coated varieties.[1] As such, the prescription of oral iron supplementation should target adequate doses of elemental iron (between 150 and 180 mg per day, given in divided doses), with enhanced gastrointestinal absorption facilitated by concomitant ascorbic acid administration and consumption on an empty stomach.[1]

References
1. Johnson-Wimbley TD, Graham DY: Diagnosis and Management of Iron Deficiency Anemia in the 21st Century. Therap Adv Gastroenterol 2011; 4(3):177–184.
2. McDiarmid T, Johnson ED: Clinical Inquiries. Are Any Oral Iron Formulations Better Tolerated than Ferrous Sulfate? J Fam Pract 2002; 51(6):576.

Answered by:
Dr. Theodore Xenodemetropoulos

7. Testing for Rubella Immunity in Pregnant Women

Could we consider a pregnant woman who tested positive for rubella in a previous pregnancy and an equivocal serology in her actual pregnancy, as being protected (or immune)?

Question submitted by:
Anonymous

Pregnant women are tested for rubella immunity to prevent congenital rubella syndrome in the newborn. Although rubella tends to be a mild affliction characterized by rash, fever, and arthralgias during the first half of pregnancy, it can cause significant cardiac, cerebral, auditory, and ophthalmic effects in the fetus. If a woman is found not to be immune in her pregnancy, she is counselled to avoid contact with rubella through the first two trimesters of pregnancy. She is then vaccinated in the postpartum period. Vaccination is safe in breastfeeding mothers but is not recommended in pregnancy, as it is a live attenuated virus.

Immunity after infection or immunization may not be lifelong, and levels can wane from one pregnancy to the next; hence, rubella immunity testing is done at each pregnancy. If a patient's serology is equivocal in a second pregnancy, she may not be protected and should be counselled to avoid potential exposure.

Answered by:
Dr. Cathy Popadiuk

8. Moulds in the Environment

What kind of air quality testing should I request for patients with medical conditions resulting from moulds?

Question submitted by:
Dr. Ailve McNestry
Vancouver, British Columbia

In general, the problem of moulds in the environment has been exaggerated. Certain moulds have the capacity to aggravate asthma, but their role in causing lung disease in people without asthma or seriously compromised immunity is not supported by the scientific literature. I do not encourage air quality testing for moulds. The companies that do the testing nearly always find something, and this then leads to expensive "remediation," which does not have any proven benefit.

Answered by:
Dr. Robert Cowie

Can ASA and Clopidogrel Be Combined for CBVD?

9.

Can ASA and clopidogrel be combined for prevention of cerebrovascular disease?

Question submitted by:
Dr. Brian Fernandes
Edmonton, Alberta

The combination of ASA and clopidogrel is not recommended based on the Management of Atherothrombosis Clopidogrel in High-Risk Patients with Recent Transient Ischemic Attacks or Ischemic Stroke (MATCH) study, published in the Lancet in 2004.[1] This study randomized 7,599 high-risk patients (with recent stroke or transient ischemic attack and at least one other risk factor for stroke) to either ASA and clopidogrel or clopidogrel alone. There was no significant benefit noted in reducing major vascular events in the combination group compared to the monotherapy group. Furthermore, there was an increased risk of life-threatening and major bleeding in the combination group.

Reference
1. Diener HC, Bogousslavsky J, Brass LM, *et al*: Aspirin and Clopidogrel Compared with Clopidogrel Alone After Recent Ischaemic Stroke or Transient Ischaemic Attack in High-risk Patients (MATCH): Randomised, Double-blind, Placebo-controlled Trial. Lancet 2004; 364(9431):331–337.

Answered by:
Dr. Sarah A. Morrow

Smoking Cessation Benefits

10.

Are the atherogenesis problems due to smoking reversible (*e.g.*, a heavy smoker who stopped 10 years prior to evaluating [framingham])?

Question submitted by:
Dr. J.D. Elltoft
Niagara-on-the-Lake, Ontario

Smoking cessation has many health benefits, including a reduction in myocardial infarction. The usually quoted statistics are that smokers have about twice the risk of coronary heart disease as non-smokers. After one year of smoking cessation, this excessive risk is minimized by half, and it disappears after 15 years.[1]

Reference
1. US Department of Health and Human Services. The Health Benefits of Smoking Cessation. US Department of Health and Human Services. Public Health Service. Center for Disease Control. Center for Chronic Disease Prevention and Health Promotion. Office on Smoking and Health. DHHS Publication No.(CDC) 1990;90–8416. http://profiles.nlm.nih.gov/ps/access/NNBBCV.pdf. Accessed: October 13, 2011.

Answered by:
Dr. Thomas W. Wilson

Protocol for Immunizing Patients

11. Could the expert comment on the protocol for immunizing a patient who, in the past, failed to complete the recommended primary series (*i.e.*, Hepatitis A, Hepatitis B, and HPV vaccines).

Question submitted by:
Dr. Aileen Comerton
Ottawa, Ontario

The problem with assessing the best course of action for people who have failed to complete the recommended vaccination protocol is that there is very little empiric data to guide these decisions. Typically, we have only small studies, in vitro data, and/or surrogate markers of protection. We do know, in general, that extending the recommended dosing intervals by a "moderate" amount is theoretically unlikely to have a significant effect on vaccine efficacy.

For Hepatitis A, there is actually modest data that suggests that when the usual two doses are given as much as five years apart (as opposed to the recommended 6 to 12 months), seroconversion is still very high. However, this is an extremely effective vaccine, and this data can not be extrapolated to other vaccines. Also, there are theoretical reasons why shortening the interval between doses is likely to reduce efficacy, and it should be avoided. New protocols for these vaccines continue to be studied. For example, there is quite good evidence for the efficacy of HBV and HPV vaccines when given to adolescents as two doses, four to six months apart. This protocol has actually been adopted in some jurisdictions. However, validation of the duration of protection, and the need for, and timing of, booster doses will have to await long-term follow-up studies. I would suggest that for any given individual, as the risk of infection with these pathogens increases, the wiser it becomes to simply restart the vaccination series and complete a "standard" protocol.

Answered by:
Dr. Michael Libman

Treating Eczema in Children

12.

What is the best way to treat eczema in a five-year-old that does not sting?

Question submitted by:
Dr. I. D'Souza
Willowdale, Ontario

When selecting therapy for active eczema, one has to realize that some common treatments can actually be quite irritating. For instance, calcineurin inhibitors often give a burning sensation when applied. This tends to settle down after a few days. While an adult may be able to accept the pain, children will often complain about it and may not allow reapplication. Furthermore, many cream formulations of steroids may sting slightly upon application due to stabilizers and preservatives. In general, ointment based treatments are less irritating. Therefore, a therapy approach that includes soothing baths, moisturizer, and an ointment-based steroid is usually the less stinging option.

Answered by:
Dr. Scott Murray

Significance of Posterior Cervical Lymph Nodes

13.

What is the significance of posterior cervical lymph nodes?

Question submitted by:
Dr. Anjali Gupta
Burlington, Ontario

In order to answer this question, we need to summarize the different groups, classifications, and drainage territories of the cervical lymph nodes. Various classifications exist for the lymph nodes of the neck. Older classifications were based on regions of the neck. The most modern is the American Head and Neck Society (AHNS) classification. It is based on six levels of the neck (and six sublevels).

- **Level I** includes the submandibular and submental nodes. It drains the oral cavity and submandibular glands
- **Level II** includes the superior internal jugular nodes. It drains the nasopharynx, oropharynx, parotid, and supraglottic larynx
- **Level III** is composed of the middle jugular nodes. It drains the oropharynx, hypopharynx, and supraglottic larynx
- **Level IV** includes the lower jugular nodes. The drainage is from the supraglottic larynx, hypopharynx, esophagus, and thyroid gland
- **Level V** is the posterior triangle area. The drainage territory is from the nasopharynx, oropharynx, and cutaneous structures of the posterior scalp and neck
- **Level VI** includes the pretracheal and paratracheal nodes. They drain the thyroid, glottic and subglottic larynx, pyriform sinus, and cervical esophagus

In summary, the posterior cervical lymph nodes are located in level V and the draining territory is described above.

A level VII also exists, but it is not mentioned here, since it involves the superior mediastinum.

Answered by:
Dr. Ted Tewfik

The Normal Reference Range for Serum Ferritin

14.

What is a normal serum ferritin?

Question submitted by:
Dr. Sliwowicz
Ajax, Ontario

The normal reference range for any laboratory value really depends on the laboratory equipment, the reagents used, and the population that is being tested. Thus, reference ranges may vary widely from laboratory to laboratory and from location to location. A specific reference range for a laboratory requires sampling from a number of people from the population of interest and determining the mean and two standard deviations from the mean. Statistically, 2.5% of the population will have values less than this range and another 2.5% of the population will have values greater than this range. At our local laboratory, the ranges for normal ferritin are 30 to 400 µg/L (adult male) and 13 to 150 µg/L (adult female). All serum ferritin values should be evaluated with the reference ranges provided by the same laboratory that performed the testing. We would encourage clinicians to become familiar with normal reference ranges of their reporting laboratory.

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

Prescribing Clopidogrel Post Angioplasty

15. Is there a correct duration to prescribe clopidogrel post angioplasty?

Question submitted by:
Dr. C. Cunningham
Vernon, British Columbia

The optimal duration of dual ASA/oral P2Y12 receptor antagonist therapy, post-stenting, particularly among drug-eluting stent (DES) recipients, is unknown. Registry data suggests a protective effect of continuing dual antiplatelet therapy beyond 24 months, but two recent randomized clinical trials did not show any benefit to continuing to take clopidogrel beyond the duration of one year.

The current Canadian guidelines recommend the following:

1) All patients who have undergone percutaneous intervention (PCI) with a bare-metal stent (BMS) should be given clopidogrel 75 mg daily in addition to ASA 75 to 162 mg daily for at least one month and up to 12 months in the absence of an excessive risk of bleeding.
2) All patients who have undergone PCI with DES implantation should be given clopidogrel 75 mg daily in addition to ASA 75 to 162 mg daily for 12 months.
3) For all post-PCI patients, indefinite therapy with ASA 75 to 162 mg daily is recommended, regardless of the type of stent.
4) Dual antiplatelet therapy with ASA 75 to 162 mg daily and clopidogrel 75 mg daily may be considered beyond one year in patients with acute coronary syndrome (ACS) who receive a BMS or DES, provided their risk of bleeding is low.
5) For patients with ACS who undergo stent implantation and have an increased risk of stent thrombosis (*e.g.*, STEMI, history of diabetes mellitus, or prior documented stent thrombosis), prasugrel 10 mg daily may be considered in addition to ASA 75 to 162 mg daily for 12 months. Prasugrel should be avoided in patients who have an increased bleeding risk, are likely to undergo coronary artery bypass graft (CABG) within seven days, have a history of stroke or TIA, are aged ≥ 75 years, or weigh < 60 kg.[1]

Reference
1. Bell DB, Roussin A, Cartier R, *et al*: The Use of Antiplatelet Therapy in the Outpatient Setting: Canadian Cardiovascular Society Guidelines Executive Summary. Can Cardiol 2011; 27(2): 208–221.

Answered by:
Dr. Brett Heilbron

Differentiating Between Corns and Warts

16. On physical exam, how would warts and corns be differentiated?

Question submitted by:
Dr. Bill Taylor
Medicine Hat, Alberta

The accurate diagnosis of warts vs. corns for the implementation of effective therapy is different for each patient. Corns tend to occur on pressure areas, have preserved skin markings, and are tender to direct pressure. Warts may occur in both pressure and nonpressure areas, interrupt skin lines, and are often tender on deep pressure (as in squeezing from the side). Also, warts usually have thrombosed blood vessels, giving them the appearance of black seeds. Corns have a smooth, glassy centre. Paring the surface of the wart or corn may reveal these differences.

Answered by:
Dr. Scott Murray

Referring to an Infertility Specialist

17. How should a family doctor work-up a couple prior to referring to an infertility specialist?

Question submitted by:
Dr. I. D'Souza
Toronto, Ontario

A thorough history and physical should be done to evaluate for potential causes of infertility, such as ovulatory defects, pelvic inflammatory disease or endometriosis in the female, or testicular problems, or a history of mumps in the male. It is important that the couple understand the concept of fertile periods and the need for frequent enough attempts at intercourse to get pregnant. Prior to referral, a semen analysis should be completed in the male and a test for tubal patency with a hysterosalpingogram should be done in the female. Evaluation for ovulatory cycles with menstrual history should also be documented. Usually, after one year of being unable to conceive, or immediately if there is an identified cause, a referral would be appropriate. As couples delay child bearing, referrals can be made sooner: after six months of unprotected intercourse at age 35 or immediately at age 40. Infertility investigations and treatments are very stressful for couples, and it is important that the family physician work with the specialist to support the couple through this emotionally charged process.

Answered by:
Dr. Cathy Popadiuk

cme