# Experts on Call

*Answers to your questions from our medical experts*

## 1. Treating Relapsing *C. Difficile*

### How do you treat relapsing *C. difficile* infection?

Submitted by: Craig Render, MD, Kelowna, British Columbia

Metronidazole (500 mg p.o. t.i.d. or 250 mg p.o. q.i.d. for 10 to 14 days) is the most commonly used first-line therapy against *C. difficile*-associated disease. Oral vancomycin (125 mg p.o. q.i.d.) should be used as first-line therapy in known hypervirulent strains causing outbreaks (the Quebec strain).

*C. difficile* recurs in 15% to 30% of cases and can be classified into re-infection or relapse. Re-infection is defined as infection with the original or new strain of *C. difficile* whereas relapse refers to return of clinical symptoms after cessation of treatment.

In both cases, patients with proven recurrent disease should be treated with oral vancomycin (250 mg p.o. t.i.d.) with tapering of the dose or pulse dosing for six weeks. Probiotic *Saccharomyces boulardii* (500 mg p.o. b.i.d. for 12 months) can be used in conjunction with vancomycin regiment to reduce recurrence. Other therapies include fecal bacteriotherapy, probiotics, IV γ-globulin and toxoid vaccine; however, the experience with these therapies remains limited at the present time.

In treating recurrent disease, it is also important to recognize the significance of patients with stool cultures positive for *C. difficile*. These positive cultures in the absence of symptoms, toxin A and/or B within the stool or *pseudomembrenous colitis* on sigmoidoscopy represent carrier state and do not require further treatment.

Resource

1. Monaghan T, Boswell T, Mahida YR: Recent Advances in Clostridium Difficile–Associated Disease. Gut 2008; 57(6):850-60.

Answered by: Dr. Anna M. Borowiec; and Dr. Robert J. Bailey



## 2. Treatment of Diabetes in Older Children

### What would be the best pharmaceutical treatment for Type 2 diabetes in older children?

Submitted by: Daniel DesRoches, MD, Gatineau, Quebec

Treatment for Type 2 diabetes in all age groups should be individualized to the treatments that best suit that particular individual. A multidisciplinary approach with lifestyle adjustments should be done with all children with Type 2 diabetes. Unfortunately, there are very few clinical trials done in children. Adult treatment principles likely can be used but are untested. Metformin likely is the medication of first choice in many and insulin also has been used. Otherwise there is only limited data with other medications.

Answered by: Dr. Vincent Woo

# 3. Indications for Combining Clopidogrel and Warfarin

## When are clopidogrel and warfarin indicated together?

Submitted by: Steve Grossman, MD, Richmond Hill, Ontario

The major indications for clopidogrel in conjunction with ASA are coronary stents (one month minimum following bare-metal stent and one year for drug-eluting stent) and following acute coronary syndrome (nine months for non-STEMI). Warfarin is indicated for prevention of thromboembolic events in patients with mechanical prosthetic valves, atrial fibrillation (AF), left ventricular thrombus and for the treatment of venous thromboembolic disease.

Some patients have an indication for dual antiplatelet therapy as well as warfarin (most commonly because of AF or anterior MI and coronary stent deployment). The risk of hemorrhagic complications is increased with this triple drug combination and the duration of administration of all three drugs should be as short as possible. For example, a patient with a mechanical valvular prosthesis or AF who has percutaneous coronary intervention should generally receive a bare-metal stent so that clopidogrel is only required for one month.

Warfarin decreases the risk of MI and there is minimal additional benefit gained by adding ASA or clopidogrel to warfarin in patients with stable coronary artery disease. Patients with anterior MI who have percutaneous coronary intervention of the left anterior descending (LAD) and have apical akinesis without definite thrombus need ASA and clopidogrel for at least one month. Warfarin is a class IIA indication (reasonable treatment, benefit probably outweighs risk) in this setting (American College of Cardiology/American Heart Association 2004 Guidelines for Management of Patients with STEMI) and there is considerable practice variation in this setting. I would limit the use of warfarin in this setting to patients with extensive apical akinesis who are at low risk of bleeding (younger patient, no NSAID use or history of GI bleed).

Answered by: Dr. Bibiana Cujec

# 4. Eczema in Dark-Skinned Children

## What is the best cream to use for severe eczema in dark-skinned children?

Submitted by: Daniel DesRoches, MD, Gatineau, Quebec

Obviously, there is no "best cream" to use for severe eczema in children with skin of colour. In addition to using proper moisturization, the options for treating severe eczema are topical corticosteroids and topical calcineurin inhibitors.

The special concern in treating children with skin of colour with topical corticosteroids is that depigmentation is a risk. The other risks of atrophy and systemic absorption with widespread use are the same in Caucasian children and children with skin of colour. Children with skin of colour frequently develop post-inflammatory hyper- or hypopigmentation due to the eczema itself and not due to the treatment and it is therefore important to treat the eczema aggressively both to control the itching but as well decreasing the inflammation lessens the development of these post-inflammatory colour changes.

The use of topical tacrolimus or pimecrolimus in children over the age of two would eliminate the risk of atrophy and depigmentation.

Tacrolimus is indicated for moderate to severe eczema and pimecrolimus for mild to moderate eczema. Practically, topical corticosteroids are still the treatment of choice for severe eczema in children of colour and it is usually necessary to use a potent (often fluorinated) topical corticosteroid to control the severe eczema. Careful monitoring in these children for atrophy and depigmentation is necessary but normally this is not an obstacle to effective treatment.

Answered by: Dr. Richard Haber

# 5. Use of Bupropion in Pregnancy

## What is the latest on the use of bupropion in pregnancy?

Submitted by: Doug Watson, MD, Calgary, Alberta

Most physicians prescribe selective serotonin reuptake inhibitors (SSRIs) to women who require antidepressant therapy during pregnancy because these drugs have been available for several years and a large body of evidence documents their safety during pregnancy. There was little safety data on bupropion until a recent study compared 2,262 infants exposed to bupropion antenatally to 4,743 infants exposed antenatally to a SSRI. No evidence was found to support any teratogenic effect associated with bupropion. Most of the exposures to bupropion were due to unintended pregnancy in individuals already taking bupropion for depression or smoking cessation. If women who do not respond to, or suffer adverse effects from SSRIs require antidepressants, available information suggests bupropion is safe.

Resources
1. Einarson A, Koren G: New Antidepressants in Pregnancy. Can Fam Phys 2004; 50:227-9.
2. Cole JA, Modell JG, Haight BR, et al: Bupropion in Pregnancy and the Prevalence of Congenital Malformations. Pharmacoepidemiology and Drug Safety 2007;16(5):474-84.

Answered by: Dr. Victoria Davis

# 6. Colon Cancer Screening Programs

## Do any provinces in Canada have active colon cancer screening programs?

Submitted by: David Stoll, MD, LaRonge, Saskatchewan

Population-based colorectal cancer programs have been launched within the last two years in Ontario and Manitoba. Plans for similar programs are actively underway in several provinces including British Columbia and Nova Scotia.

Answered by: Dr. Sharlene Gill

# 7. Risks of Tegaserod

## Can tegaserod be used beyond the recommended 12-week period? What are the risks associated with long-term use?

Submitted by: Jennifer Lush, MD, Victoria, British Columbia

Tegaserod is a serotonin 5-HT4 receptor partial agonist that primarily works on stimulating the motility of the digestive tract. Its main indication is for irritable bowel disease with predominant constipation features and for chronic constipation. On March 30, 2007, tegaserod was withdrawn from the Canadian market due to safety concerns about an increase in CV events including increased risk of strokes and MIs. Therefore, patients still currently on tegaserod are recommended to discontinue the use of this product.

Answered by: Dr. Richmond Sy



See prescribing summary and study parameters on page 129

# 8. The Best Treatment for Tremor

## What is the best treatment for tremor associated with mood stabilizers and anticonvulsants?

Submitted by: Philip Severy, MD, North Vancouver, British Columbia

The most common tremor associated with mood stabilizers is seen with lithium therapy. It is a benign postural tremor that worsens during activities requiring fine motor control; it can be socially embarrassing and occupationally troublesome. This benign tremor often improves spontaneously, but if it does not, benefit may be obtained from dose reduction, use of a slow-release lithium preparation, elimination of dietary caffeine and treatment of associated anxiety. Medications useful in treating lithium tremor include primidone and β-adrenergic receptor antagonists such as propranolol. With long-term lithium therapy, a tremor with parkinsonian characteristics may occasionally occur. A severe tremor at any time during the course of lithium therapy may be an indication of lithium intoxication.

Among anticonvulsants used as mood stabilizers, valproate is known to occasionally cause tremor as a side-effect. The tremor happens more frequently when valproate is combined with lithium or serotonin reuptake inhibitors. This tremor can often be controlled by β-adrenergic receptor antagonists, such as propranolol.

Answered by: Dr. Hany Bissada

# 9. Lasers in Cosmetic Spas vs. Physician's Offices

## Are lasers in cosmetic spas the same as those found in a physician's or dermatologist's office?

Submitted by: Roger Lan, MD, Bathurst, New Brunswick

Lasers are a surgical tool used to treat a variety of skin diseases, including cosmetic concerns. There are many indications and many effective types of lasers for each indication. These include laser hair removal (most commonly performed laser procedure), laser skin resurfacing, vascular lesion treatment, pigmented lesion treatment, tattoo removal and laser-mediated photodynamic therapy.

Lasers have a number of potential side-effects including immediate local erythema, pain and swelling, pigmentary changes (post-inflammatory hyperpigmentation and hypopigmentation), scarring and infections.

Lasers are available (*e.g.*, can be sold) to nearly all healthcare practitioners, including "cosmetic spas." However, it is not the laser that makes the difference in most cases, rather it is the skill and experience of the operator. Lasers should only be used by physicians and physician assistants who are skilled in their use. If laser therapy is indicated, ensure you refer patients to safe, reliable clinics you trust.

Answered by: Dr. John Kraft; and Dr. Charles Lynde

# 10. NSAID Use and Recurrent Tinnitis

## Is there any cause for concern with NSAID use in someone with recurrent tinnitis and deafness (unilateral)?

Submitted by: P. Hawley, MD, North Vancouver, British Columbia

NSAIDs constitute a heterogenous group of compounds that have therapeutic actions and side-effects similar to those of salicylates. Most NSAIDs act as analgesics and anti-inflammatories by inhibiting cycloxygenase pathways with a resultant decrease in prostaglandin synthesis. Since these drugs can be obtained without prescription, they are potentially available for long-term use and abuse.

One of the reported side-effects of many NSAIDs is ototoxicity, manifesting as mild to moderate, usually reversible, hearing loss and tinnitus. Chapman in 1982 reported a series of five patients who sustained hearing loss with naproxen; two recovered their hearing after discontinuing the drug. Sudden and permanent sensorineural hearing loss (SNHL) has rarely been reported as a result of NSAID use. This has generally been in the context of patients with underlying renal dysfunction, rheumatoid arthritis, polyarteritis nodosa, advanced age, or the use of NSAIDs with other potentially ototoxic medications.

The classic description of salicylate-induced SNHL is one of a mild to moderate bilateral symmetrical loss, which may be flat or only in the higher frequencies. The hearing loss is typically reversible and recovery usually occurs 24 to 72 hours after cessation of the drug. Salicylate-induced tinnitus has been characterized as tonal and pitch matching has identified the tinnitus frequencies to be usually around 7 kHz to 9 kHz. Clinically, the onset of tinnitus has been used as the earliest manifestation of toxicity.

The mechanisms of naproxen's ototoxic effects have been suggested to be similar to those described for salicylates. Salicylates and NSAIDs have been shown to increase levels of norepinephrine, decrease concentrations of prostaglandins and increase leukotrienes in the perilymph. Decreased blood flow and cochlear hemorrhage (which may be influenced by catecholamines and arachidonic metabolites) have been suggested as occurring in salicylate and NSAID ototoxicity. However, Koopman and colleagues found no alterations in the auditory brainstem responses of guinea pigs after long-term ibuprofen treatment. Morrison and Blakely noted no ultrastructural abnormalities in guinea pigs treated with indomethacin except for a questionable distension of Reissner's membrane.

Taking into account the available literature, recurrent tinnitus and deafness in the context of NSAID administration are symptoms that should provoke caution. Tinnitus may herald an impending hearing loss. Although unilateral deafness is less likely to result from otoxicity than a bilateral hearing deficit, discontinuation of the NSAID should be considered and the patient's hearing monitored for improvement. Particular care should be observed in those patients with underlying renal disorders or autoimmune conditions.

Answered by: Dr. Emma Barker; Dr. Sanjay Verma; and Dr. Jonathan Irish

# 11. The Role of ACE Inhibitors in Renal Failure

## What is the role of ACE inhibitors in renal failure?

Submitted by: David C. Lim, MD, Toronto, Ontario

ACE inhibitors inhibit the conversion of renin to angiotensin to aldosterone with the most notable effect being impairment of efferent arteriole vasoconstriction. This results in decreased glomerular pressure and subsequent decreases in proteinuria, glomerular sclerosis and decreases in systemic BP. In acute renal failure, ACE inhibitors (or ARBs) should be held as they decrease glomerular filtration rate (GFR) and may exacerbate the renal impairment. In chronic renal failure (CRF), ACE inhibitors and ARBs are the mainstay of therapy as multiple randomized controlled trials have demonstrated preservation of renal function with ACE inhibitors. The renoprotective effects of ACE inhibitors occur in multiple different populations, namely patients with proteinuria, diabetes and hypertension. They are also protective in patients who lack proteinuria but have CRF, normotensive patients with CRF and patients with severe renal impairment (cr 200 to 300). African Americans seem to have a blunted response to ACE inhibitors and are the only group lacking a demonstrable benefit (African-American Study of Kidney Disease).

Resource

1. Wright JT Jr, Bakris G, Greene T, et al: Effects of BP Lowering and Antihypertensive Drug Class on Progression of Hypertensive Kidney Disease. JAMA 2002. 288(19):2421-31.

Answered by: Dr. Manish Sood

# 12. Screening in Hodgkin's Survivors

## What are the recommended cancer screening tests for a 30-year-old post Hodgkin's Disease survivor?

Submitted by: Anne Sorensen, MD, Oshawa, Ontario

While risk of relapse largely depends upon the stage at presentation, most young patients with Hodgkin's lymphoma are cured with treatments and thus, a significant emphasis during follow-up is placed upon preventive and early recognition strategies for any rare long-term, toxic effects from their treatments. Therefore, individual recommendations depend upon the extent of disease at presentation and treatment received. Clarification of recommended follow-up should be obtained from the treating hematologist/oncologist when possible.

As a minimum general guideline, it is recommended that patients should be examined every three months for two years post-treatment, every six months for three years, then annually including examination of lymph nodes, thyroid, breast, abdomen and skin along with a complete blood count and alkaline phosphatase and a chest x-ray. Prior radiation to the neck warrants careful dental care (for risk of dental caries due to decreased salivation) and thyroid examination with annual TSH (risk of hypothyroidism and secondary thyroid cancer after irradiation). Mammography starting 10 years after diagnosis or age 400 (whichever comes first) and pap smears are recommended. Immunizations should be up-to-date including influenza vaccination every year, pneumococcal vaccine every five years and tetanus/diphtheria every 10 years.

Resource
1. www.bccancer.bc.ca

Answered by: Dr. Sharlene Gill

*A significant emphasis during follow-up is placed upon preventive and early recognition strategies for any rare long-term toxic effects from their treatments.*

# 13. Subarachnoid Hemorrhage Headache

## What are the characteristics of the headache of subarachnoid hemorrhage and how do you work it up?

Submitted by: Anonymous

The headache of subarachnoid hemorrhage (SAH) is generally described as a sudden onset, (to maximum severity within usually less than one minute), extremely severe headache (patients will state it rates 10/10 on an impromptu pain scale). The patient generally states that it is the worst headache of their life, with some describing it "as if someone took a sledgehammer to the back of [their] head." In a typical case, the headache will stay at its maximum for at least a number of hours. It can also be accompanied by a number of associated features:

- Nausea and vomiting
- Stiff neck (meningismus)
- Decreased level of consciousness
- Retinal hemorrhages
- Focal neurologic signs (*e.g.*, cranial nerve palsies, lateralized weakness)
- Occasionally seizure, confusional state, history of trauma (traumatic SAH)

If a person presents with these symptoms or signs, usually to the ER, then the first step is to get an unenhanced CT scan of the brain. If the scan is negative for SAH, then the next step is to do a lumbar puncture (LP). This must be done carefully, with fluid from both the first and last tubes taken sent for red blood cell (RBC) count and another sent for xanthochromia (this is an indirect measure of lysed RBCs. It becomes positive after about 12 hours and stays positive for two to three weeks). If the LP is abnormal or equivocal, or the initial CT-scan without contrast is positive, then the patient should be sent for cerebrovascular imaging, such as CT angiography, or cerebral angiography. If this imaging is negative, then repeat cerebrovascular imaging in one to three weeks and imaging of the brain and spinal cord is indicated. This is to rule out aneurysms that were hidden due to early vasospasm and parenchymal lesions that can bleed (*e.g.*, small arteriovenous malformations [AVMs]).

Resource
1. Suarez JI, Tarr, RW, Selman WR: Aneurysmal Subarachnoid Hemorrhage. N Engl J Med 2006; 354(4):387-96.

Answered by: Dr. Inge Loy-English

# 14. Depression vs. Demoralization

## How does one differentiate depression from demoralization?

Submitted by: Paul Jurgens, MD, Abbotsford, British Columbia

Depression is a medical/psychiatric diagnosis that is made by a physician when the patient's presentation meets specific criteria as described in the Diagnostic and Statistical Manual of Mental Disorders (DSM IV). Demoralization, on the other hand, is not a diagnosis but a lay person term that implies that a person has lost his/her ambition and optimism about life, usually as a reaction to a major psychosocial loss such as a marriage break-up. If the demoralization is severe enough to impair the professional and social functioning of the patient, then the medical/psychiatric term to use would be an adjustment disorder. Understandably, the symptoms of depression may overlap with the presentation of an adjustment disorder with a depressed mood and certainly an adjustment disorder can progress to a full depression in some individuals.

An adjustment disorder is expected to resolve completely within six months from the termination of the psychosocial stressor, if not, then a diagnosis of depression is warranted.

Resource
1. Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision (DSM IV-TR).

Answered by: Dr. Hany Bissada

# 15. Cancer Risk for Ex-Smokers

## What are the statistics on lung cancer risk for someone who quit smoking 20 years ago? Does their risk return to near the general population risk?

Submitted by: George Linn, MD, Kingston, Ontario

There is indisputable evidence that cigarette smoking causes lung cancer and is the major risk factor for the vast majority of lung cancer deaths in North America.[1] The risk for lung cancer in a smoker is 10 to 20 times that of a lifelong non-smoker. Smoking cessation is associated with a decline in relative risk for development of lung cancer as the duration of not smoking increases. However, even with the longest durations of quitting studied, the risks for lung cancer remain greater in former smokers compared with lifetime non-smokers.[1] This can be explained because the absolute risk of lung cancer does not decline following cessation, but the additional risk that comes with continued smoking is avoided. Therefore, the increased relative risk of lung cancer 20 years after smoking cessation would depend on host susceptibility factors and the duration and amount of cigarette smoking prior to that critical juncture.

Reference
1. The Health Consequences of Smoking: A Report of the Surgeon General. [Atlanta, Ga.]: Dept. of Health and Human Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health; Washington, D.C. US G.P.O., 2004.

Answered by: Dr. Paul Hernandez

# 16. Duct Tape in Wart Treatment

## Are there studies supporting duct tape in adult wart treatment?

Submitted by: **Erik Cunningham, MD,** Victoria, British Columbia

Use of duct tape in treating warts reminds one of the adage "use a new treatment quickly before it is proven not to be effective."

The media coverage for duct tape treatment of common warts (verruca vulgaris) stems from a six-week study of pediatric patients by Focht, *et al* in 2002 which showed warts treated with duct tape responded better than warts treated with liquid nitrogen cryotherapy. Eighty-five per cent of the duct tape treated patients had complete resolution of their warts vs. 60% in the cryotherapy treated patients. This study has been criticized because of small number of subjects, large loss to follow-up and some telephone follow-up, method of application of cryotherapy (10 seconds only) and lack of a placebo arm.

A 2006 randomized placebo-controlled trial from the Netherlands of children aged four to 12 treated for six weeks with duct tape vs. corn pads (placebo) for verruca vulgaris showed the duct tape treatments to be no more effective than placebo.

A 2007 double-blind randomized controlled trail of adults treated for eight weeks with duct tape vs. moleskin (placebo) for common warts also showed no statistical difference between duct tape and moleskin in treating warts.

# 17. The Best Treatment for Tinea Versicolor

## What is the best treatment for tinea versicolor?

Submitted by: Bruno Tremblay, MD, Canton-de-Hatley, Quebec

Tinea versicolor, or pityriasis versicolor, refers to a yeast infection of the skin caused by normal lipophilic yeast skin flora of the genus *Malassezia*. It is found throughout the world affecting all ages and sexes. It presents with brown-yellow to pink hyper or hypopigmented thin plaques with a light scale particularly in sebaceous areas (*e.g.*, back, chest, scalp). Hypopigmentation is thought to result from yeast metabolites interfering with melanocyte function or decreased tanning due to the ability of the yeast to filter sunlight. It is often asymptomatic and patients are frequently concerned regarding the appearance.

Antimycotic shampoos (*e.g.*, 2.5% selenium sulfide shampoo, zinc pyrithione, or ketoconazole 2%) are often successful. It is often helpful to treat all skin from the neck to the knees. Shampoos should be left on the skin for five to 10 minutes before washing off. This should be done daily for one to two weeks. It can be repeated on the first and third day of each month thereafter for six months to help prevent recurrence. Patients should be advised that despite complete mycological cure, pigmentary changes may not resolve for months.

Topical antifungal creams (*e.g.*, ketoconazole 2%, terbinafine, ciclopirox 0.1%) are also effective. They should be applied once or twice daily for one to two weeks.

For more extensive cases, or if topical therapies are not effective, a short course of oral azole antifungal therapy is often used. However, they must be used with caution, due to their risk of hepatoxicity and serious drug interactions. The main advantages of oral azole therapy include a very high cure rate and ease of administration for the patient. Options include ketoconazole 400 mg p.o. for one dose, fluconazole 300 mg p.o. once weekly for two weeks, itraconazole 200 mg p.o. q.d for five to seven days. Oral terbinafine is not effective for pityriasis versicolor as it is not excreted in the sweat glands.

Recurrences can be common, especially in hot, humid climates (up to 60% in first year and 80% in second year). Antifungal shampoos or topical antifungals used several days each month may be helpful, but resistance may be emerging in some *Malassezia* species. For more details, see resources for a review on pityriasis versicolor.

Resources

1. Schwartz RA: Superficial Fungal Infections. Lancet 2004; 364(9440):1173-82.

Answered by: Dr. Charles Lynde; and Dr. John Kraft

# 18. Neonatal Complications for Mothers with Lupus

## What complications can arise from in the neonatal period to a child born of a mother with lupus?

Submitted by: R. Strachan, MD, Winnipeg, Manitoba

Neonatal lupus syndrome (NLS) is a rare disorder caused by the transplacental passage of maternal antibodies. Only 1% of infants with positive maternal antibodies will develop NLS; most common clinical manifestations are cardiac, dermatologic and hepatic. Congenital heart block (CHB) is associated with maternal antibodies to RO (SS-A) and La (SS-B) and is usually diagnosed between 18 and 24 weeks. Mortality approaches 30% and 57% of surviving children require pacemakers. Cutaneous findings are transient; two-thirds are present at birth with the remainder developing within the first two to five months of life. Hematologic disturbances (*e.g.*, hemolytic anemia, profound thrombocytopenia, neutropenia) may occur in the first two weeks of life and disappear by the end of the second month. Hepatobiliary diseases can vary from elevations of aminotransferase levels to conjugated hyperbilirubinemia with normal or slightly elevated aminotransferase levels.

In children with cutaneous involvement, especially males, hematologic and hepatic disease may be as common as the cardiac disease and therefore infants should be evaluated for these disorders.

Resource

1. Friedman DM, Rupel A, Glickstein J, et al: Congenital Heart Block in Neonatal Lupus: The Pediatric Cardiologist's Perspective. Indian J Ped 2002; 69(6):517-22.

Answered by: Dr. Victoria Davis

# 19. Fasting Before a Serum Lipid Profile

## How important is fasting to check cholesterol and triglycerides? Is a 14 hour fast better than an eight hour fast?

Submitted by: Denis Petrunia, MD, Victoria, British Columbia

A standard serum lipid profile consists of total cholesterol, triglycerides and HDL-C. Lipoprotein analysis should be performed after 12 to 14 hours of fasting to minimize the influence of postprandial hyperlipidemia. There is little change in HDL-C and total cholesterol (TC) in non-fasting samples. However, triglycerides are elevated after a meal, especially if it is high in fat. The LDL-C is indirectly calculated from the triglycerides: LDL-C = TC - VLDL-C - HDL-C (where VLDL-C is assumed to be one-fifth of the total triglyceride concentration). Therefore, to obtain an accurate LDL-C calculation, the patient should fast for a minimum of 12 hours.

Lipid and lipoprotein concentrations and composition may be markedly perturbed by the acute phase response that is associated with an acute MI, surgical trauma, or infection. Tissue injury generates acute phase proteins that impair hepatic lipoprotein production and metabolism. This can reduce serum concentrations of TC, HDL-C, LDL-C and apolipoproteins B and A-I. A fasting lipid profile should be obtained within 24 hours of a patient's admission to hospital or a minimum of one month following discharge to obtain a representative LDL-C level.

Answered by: Dr. Bibiana Cujec

# 20. Safety of the New COX-2 Inhibitors

## How safe are new COX-2 inhibitors (*e.g.*, lumiracoxib)?

Submitted by: Charles Anderson, MD, Upper Tantallon, Nova Scotia

Currently in Canada, the only COX-2 inhibitor available on the market is celecoxib whose CV safety profile has been shown to be comparable to non-selective NSAIDS such as naproxen. Celecoxib is still widely used and well tolerated by patients and should be used preferentially in the setting of peptic ulcer disease, chronic anticoagulation and GI intolerance. Meloxicam may have COX-2 selectivity at lower doses; however, when used at higher doses, it becomes non-selective, as evidenced by the increased risk of GI bleeding.

Lumiracoxib was briefly on the Canadian market in 2007 and was billed as a "heart safe" selective COX-2 inhibitor. However, it was taken off the market in 2007 because of serious concerns regarding hepatotoxicity, based on reports of fatalities related to fulminant hepatic failure in Australia and two cases of drug-related hepatitis in Canada. Lumiracoxib was never approved in the US and has since not been granted approval secondary to this reported risk of hepatotoxicity.

Answered by: Dr. Michael Starr; and Dr. Sabrina Fallovallita

# 21. Using Paroxetine for Premature Ejaculation

## It has been said that paroxetine can be used to treat premature ejaculation. What is the dose and when is it to be administered? Can you comment on the effectiveness? Any alternative treatments?

Submitted by: Shannon Davidson, MD, Barrie, Ontario

Paroxetine can be used to treat premature ejaculation either with single dosing prior to sexual relations or by achieving a blood level through daily use. The first option decreases the side-effects, but does not work for all patients. Initial dosing should be 10 mg and it can afterwards be elevated to 20 mg. If this drug does not work, other selective serotonin reuptake inhibitors can be tried. Other options should include sexotherapy, use of a condom and the use of desensitizing cream. If erectile dysfunction is present, a PDE-5 inhibitor such as sildenafil could also be administered.

Answered by: Dr. Hugues Widmer

# 22. Frequency of Bloodwork in an Epileptic Patient

## For the epileptic patient who has been stable on carbamazepine for many years, how often should bloodwork be done and what specifically should be checked?

Submitted by: Danielle Fisch, MD, Canton-de-Hatley, Quebec

First, if a person has been stable and seizure free for many years, one should have a discussion with the patient about a trial of discontinuation of the medication. They may not need it anymore. However, the discontinuation should be very slow (over two to three months, depending on the dose they are on) and precautions would need to be taken during discontinuation, such as no driving when weaning off.

If they elect to stay on the medication and if they are healthy and stable, bloodwork should be done once per year. If they have concomitant medical problems, I would do the bloodwork every three to six months, depending on the nature of their illness. This should include:

- Complete blood cell count (neutropenia)
- Electrolytes (hyponatremia)
- Thyroid stimulating hormone (hypothyroidism)
- Liver function tests (transaminitis)
- Blood urea nitrogen/creatinine and a urinalysis (renal dysfunction)

Also, a periodic vision exam should be done, as there is a small risk of glaucoma. A recent Cochrane review has shown that there is no utility in doing routine drug levels on a stable patient, with no symptoms or side-effects and no change in seizures.

Answered by: Dr. Inge Loy-English

# 23. Adding Fibrate to a Statin

## When to add fibrate to a statin?

Submitted by: Martyn Chilvers, MD, Sarnia, Ontario

Generally speaking, combination therapy for dyslipidemia is used for individuals at high risk who are not reaching targets. There are very few studies assessing this combination. The Fenofibrate Intervention and Event Lowering in Diabetes (FIELD) study was a lipid-lowering study in patients with Type 2 diabetes using fenofibrate; however, there were a sizeable portion of the study patients who used statins as well. The safety of the combination was confirmed in this study. The Action to Control Cardiovascular Risk in Diabetes (ACCORD) study in high-risk individuals with Type 2 diabetes will specifically assess the combination vs. a statin alone. Therefore, this combination should be considered if target lipid levels are not being met or if triglyceride levels are very high in a high-risk CV patient placing the patient at significant risk for pancreatitis. Dx

Answered by: Dr. Vincent Woo