1. Stroke Prevention in Patients with PFO

What is the primary prevention of stroke in a patient with patent foramen ovale (PFO)?

Submitted by: J. Timothee, MD, St. Lambert, Quebec

Patent foramen ovale (PFO), a small, slit-like flap in the atrial septum, is found in about 20% of adults. PFO is associated with increased risk of stroke in patients under 55-years-of-age. This is likely due to a paradoxical embolism of small clots that form in the leg veins. Most patients with PFO do not have any associated problems (*e.g.*, stroke, hypoxemia) and no specific therapy for primary prevention of stroke is required.

We do not know the best therapy for a patient who has a stroke, but does not have any other potential cause other than a PFO (*i.e.*, for secondary prevention of recurrent stroke). Some studies have found that certain features associated with PFO, such as atrial septal aneurysm or a wider opening of the PFO, may increase the likelihood of recurrent strokes, but this has not been confirmed in other studies. Although it is tempting to percutaneously close a PFO in a young patient who has had a stroke or transient ischemic attack, we do not know if this is the best therapy. Recurrent strokes have been reported after PFO closure. Current guidelines recommend acetylsalicylic acid in patients with PFO who have had a stroke, and warfarin if the patient has a documented deep vein thrombosis or hypercoagulable state. If possible, the patient who has had a stroke and is found to have a PFO should be enrolled in one of several ongoing clinical trials of percutaneous PFO closure. Only through these clinical trials can we determine the optimal therapy of patients with both PFO and stroke.

Answered by: Dr. Bibiana Cujec

Patent foramen ovale is associated with increased risk of stroke in patients under 55-years-of-age. This is likely due to a paradoxical embolism of small clots that form in the leg veins.

2. Differentiating Between IBS and IBD

Please elaborate on the difference between IBS and IBD, and how to differentiate between the two.

Submitted by: Anna-Viola Dugas, MD, Bathurst, New Brunswick

Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD) are two separate entities, though overlap between the two can occur. Differentiation between these two conditions can be made based on careful history and physical examination, with tailored laboratory and investigative testing.

IBS is part of the spectrum of functional gastrointestinal disorders, characterized primarily by chronic, recurrent abdominal pain and altered bowel habits, in the absence of organic pathological changes. Though the pathophysiology is not entirely clear, proposed mechanisms include abnormalities in: gastrointestinal motility, sensation, autonomic function, and serotonin pathways. The Rome III Criteria for diagnosis of IBS requires that patients have recurrent abdominal pain or discomfort at least three days per month, during the past three months, associated with two or more of:

- Improvement with defecation
- Onset associated with change in frequency of stool
- Onset associated with change in form (appearance of stool)

This must occur in the absence of warning signs (*e.g.*, anaemia, rectal bleeding, weight loss, fever, age > 50, family history of colon cancer or major change in symptoms), which would warrant investigation for organic etiology. Based on evaluation of bowel habits and stool characteristics, patients can be classified into one of three subsets: diarrhea-predominant IBS, constipation-predominant IBS or mixed subtype.

In contrast, IBD – which includes ulcerative colitis (UC) and Crohn's disease – is characterized by inflammation of the mucosal lining of the gastrointestinal tract. The pathophysiology is thought to be multifocal, with both genetic predisposition, and an autoimmune response to a pathologic organism or intraluminal antigen each playing a role. Clinical history typically includes diarrhea (with or without the presence of blood), abdominal pain, tenesmus, weight loss and, in the case of complicated Crohn's, symptoms of obstruction or perianal disease. Extraintestinal manifestations such as arthritis, uveitis and dermatologic conditions can be found with both UC and Crohn's. Furthermore, IBD is associated with an increased risk of gastrointestinal malignancy.

Differentiation between the two conditions can be made by the clinical history, and laboratory findings, which in IBD may include anaemia, increased C-reactive protein, and sometimes leukocytosis. However, the distinguishing factor of IBD is the presence of organic changes: colonoscopy is remarkable for inflammation, erythema, exudates, and ulceration. Microscopic findings of biopsies in IBD feature neutrophilic inflammation, with the presence of crypt abscesses in UC or granulomas in Crohn's disease. In contrast, colonoscopy in IBS will not show any pathologic abnormalities, as this is purely a functional disorder.

References
1. Grundmann O, Yoon, SL. Irritable Bowel Syndrome: Epidemiology, Diagnosis and Treatment: An Update for Health-care Practitioners. J Gastroenterol Hepatol 2010;25(4):691-9.
2. Mayer EA. Clinical Practice: Irritable Bowel Syndrome. N Engl J Med 2008;358(16):1692-9.
3. Baumgart DC, Sandborn WJ. Inflammatory Bowel Disease: Clinical Aspects and Established and Evolving Therapies. Lancet 2007;369:1641-57.

Answered by: Dr. Robert Bailey and Dr. Marta McCrum

3. Use of BCP After Delivery

? At what time can a woman take birth control pills after delivery, if she is breast feeding (and has no period)?

Submitted by: Samir Abouna, MD, Mississauga, Ontario

Combined (estrogen and progesterone) contraception can decrease breast milk production, especially if production is not well established, therefore, it is not usually started until six weeks postpartum. If the woman is not breastfeeding, combined contraception can be started at three weeks postpartum. The progesterone-only pill does not affect milk supply; it is an excellent option for breastfeeding mothers, and may be started at three weeks postpartum. The latter option is slightly less efficacious than combined contraception, however, when combined with the decreased fertility associated with breastfeeding (especially exclusive breastfeeding) efficacy is similar to that of combined contraception.

Reference
1. Black A, Francouer D, Rowe T, et al. Canadian Contraception Consensus. J Obstet Gynaecol Can 2004 Feb;26(2):143-56,158-74.

Answered by: Dr. Victoria Davis

4. Bisphosphonates in Asymptomatic, Postmenopausal Women

What evidence is there to use bisphosphonates in asymptomatic, postmenopausal women with osteopenia and no major risk factors?

Submitted by: Anita Srivastava, MD, Toronto, Ontario

Osteopenia is defined as a bone mineral density (BMD) T-score of -1.0 to -2.4. One study extracted data on postmenopausal women with osteopenia and no previous fracture from four randomized studies of risedronate versus placebo. The pooled results showed that risedronate given over three years decreased the risk of fracture from 6.9% to 2.2%.[1] Clearly, the number of women needing treatment in such a category is large, and another study found that treating this group of patients with bisphosphonates was not cost-effective.[2] Importantly, physicians who treat bone fragility are moving away from using BMD as the sole determinant for treatment. Algorithms that consider BMD, as well as other independent risk factors for fracture, such as age and previous fracture, have been developed that estimate the patient's 10-year risk. Evidence supports pharmacologic treatment of patients with a 20% 10-year risk of any fracture, or 3% risk of hip fracture.[3] In the question above, if the patient is a 60-year-old Caucasian female who has a height of five feet, weight of 120 pounds, BMD T-score at the hip of -2.0, and no other risk factors, her 10-year risk of any fracture is 12%, and risk of hip fracture is 2%; therefore, treatment with bisphosphonates is not clearly indicated. Vitamin D and calcium, as well as certain lifestyle modifications, would be reasonable treatments for osteopenic patients in whom pharmacotherapy is not indicated.

References
1. Siris ES, Simon JA, Barton IP, et al. Effects of Risedronate on Fracture Risk in Postmenopausal Women with Osteopenia. Osteoporos Int 2008 May;19(5):681-6.
2. Schousboe JT, Nyman JA, Kane RL, et al. Cost-effectiveness of Alendronate Therapy for Osteopenic Postmenopausal Women. Ann Intern Med 2005 May 3;142(9):734-41.
3. Rahmani P, Morin S. Prevention of Osteoporosis-related Fractures Among Postmenopausal Women and Older Men. CMAJ 2009 Oct 19;181(11):815-20.

Answered by: Dr. Michael Starr and Dr. Emil Nashi

5. RTMS for Migraines

Is repetitive transcranial magnetic stimulation (RTMS) good for migraines?

Submitted by: Jean-Guy Gagnon, MD, Sudbury, Ontario

Repetitive transcranial magnetic stimulation (RTMS), has shown some beneficial effects in the treatment of chronic and neuropathic pain, as well as in some neurological and psychiatric disorders. High-frequency RTMS increases, and low-frequency RTMS decreases, neural excitability. As there is evidence of neuronal hyperexcitability in migraines, it is thought that low-frequency RTMS may decrease migraine headaches. One small pilot study claimed prophylactic effects of high-frequency RTMS in migraine. Another study with low-frequency RTMS did not show any significant difference in the number of migraine attacks when compared with the placebo group; there was also no significant improvement in the number of days and total hours with migraine, pain intensity and use of analgesics. However, the different studies have reported controversial results; there have been some reports demonstrating positive effects of RTMS on the number of migraine attacks, and days and total hours with migraine, in some groups of patients. These results are encouraging, and indicate that further research in this area is needed.

Answered by: Dr. Abdul Qayyum Rana

6. ABRS versus Viral Rhinitis

How do you differentiate acute bacterial rhinosinusitis from viral rhinitis, and what are the management guidelines?

Submitted by: Sandi Frank, MD, Edmonton, Alberta

The symptoms of acute bacterial rhinosinusitis (ABRS) are facial pain, sinonasal blockage and congestion, anosmia, mucopurulent rhinorrhea, fever, post-nasal drip, maxillary dental pain, ear fullness and fatigue. Many of these symptoms can be present in viral rhinitis, sometimes making correct diagnosis difficult. Facial pain and mucopurulent discharge are less prominent with a viral aetiology. Although sinusitis may be a sequelae of viral rhinitis, bacterial superinfection is thought to occur in less than 2% of cases of viral rhinosinusitis. Viral rhinitis may also be associated with other "common cold" symptoms, such as throat pain, sneezing and malaise. Examination may reveal purulent discharge, or post-nasal drip and facial tenderness in patients with ABRS.

Saline sprays help clear secretions and provide some symptomatic relief, and can be used for viral or bacterial rhinosinusitis. Viral rhinosinusitis does not require antimicrobial treatment. ABRS usually settles without treatment, but if symptoms last longer than seven days, antibiotics should be considered. They should be combined with some form of decongestant and regular saline sprays. In the immunocompetent, normally healthy patient, it is generally safe to wait five to seven days before considering antimicrobial treatment if you initially suspect a viral aetiology.

Amoxicillin/Clavulanate is my recommended first choice in this scenario. There are many other antimicrobials to consider for patients with penicillin allergy, or second line therapy including azithromycin, clindamycin and doxycycline. There is mixed evidence on the use of topical corticosteroids in the acute setting, but systemic corticosteroids may aid decongestion if antibiotics and saline sprays are not working to relieve symptoms. Nasal decongestants may be used for short periods only. Antihistamines are not indicated.

Complications of acute sinusitis include periorbital cellulitis, meningitis, intracranial abscess and cavernous sinus thrombosis. These are rare, but they clearly warrant antibiotic treatment and expert management. Surgery is rarely necessary for ABRS, but is often required for complicated disease, or persistent sinusitis with severe symptoms that fails to respond to maximal medical therapy.

Special consideration is warranted in patients with immunodeficiency, ciliary dyskinesia, cystic fibrosis or a history of chronic rhinosinusitis or polyposis. A lower threshold for treatment and specialist referral is required for these patients. Referral to an otolaryngologist should be considered for persistent, severe ABRS not responding to medical management, chronic rhinosinusitis (symptoms lasting longer than 12 weeks) and the presence of complications.

Answered by: Dr. Ben Dixon

7. Clues to Diagnose Bipolarity

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

Submitted by: Waguin Tannous, MD, Montreal, Quebec

Each of the following features, particularly when they exist in combination, may be predictive of bipolar disorder:

- Onset of depressive or hypomanic/manic symptoms at an early age
- Psychotic depression before 25-years-of-age
- Postpartum depression, especially one with psychotic features
- Rapid onset and offset of depressive episodes of short duration (less than three months)
- Recurrent depression (more than five episodes)
- Depression with marked psychomotor retardation
- Atypical features (reverse vegetative signs)
- Seasonality
- Bipolar family history
- Trait mood lability (cyclothymia)
- Hyperthymic temperament

A trial of SSRI can lead to a manic or hypomanic switch if given to a bipolar disorder patient with any of the following:

- Prior history of switches to mania on antidepressant medications
- Rapid cycling history
- Onset of depression at a young age, particularly a prepubertal onset of depression
- Mixed depression with racing thoughts

Resource
1. Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th ed. Chapter 13.

Answered by: Dr. Hany Bissada

8. Hepatitis B and C Testing

Please comment on hepatitis B and C testing.

Submitted by: David Stevens, MD, Victoria, British Columbia

Hepatitis B

The table below summarizes the key serologic markers that help determine whether a person has an acute, resolving or chronic infection with the hepatitis B virus. In addition, the table provides a summary of whether a person is immune due to a resolved infection or through vaccination. An extensive discussion about this matter may be found in the chapter on hepatitis B in the Canadian Guidelines on Sexually Transmitted Infections, 7th Edition (2006).

Hepatitis C

The serologic tests that are available for detection of hepatitis C virus (HCV) infection include the anti-HCV. This indicates past or present infection, but does not differentiate between acute, chronic and resolved infections. The presence of anti-HCV antibodies should lead to additional supplemental, or confirmatory testing.

Reference
1. Modified from: Canadian Guidelines and Sexually Transmitted Infections, 7th ed. 2006.

Answered by: Dr. John Embil

Table 1
Serologic Markers for Hepatitis B Virus[1]

Stage	HBsAg	HBeAg	Anti-HBc IgM	Anti-HBc IgG/total	Hepatitis B Viral DNA	Anti-HBs
Acute (early)	+	+	+	+	+	–
Acute (resolving)	+	–	+	+	–	–
Chronic	–	+/–	–	+	+/–	–
Resolved	–	–	–	+	–	+/–*
Vaccinated	–	–	–	–	–	+*

Anti-HBc = antibody to hepatitis B core antigen
Anti-HBs = antibody to hepatitis B surface antigen
HBeAg = hepatitis B early antigen
HBsAg = hepatitis B surface antigen
+ = present; – = absent
* In some patients, anti-HBs may decline over time and become undetectable

9. Reversal of Peripheral Neuropathy

Is peripheral neuropathy, seen with diabetes mellitus and hyperthyroidism, reversible with better glycemic control and thyroid replacement?

Submitted by: K. Roeck, MD, North Vancouver, British Columbia

The most common form of neuropathy with diabetes mellitus (DM) and hypothyroidism is a distal sensory symmetric polyneuropathy. In DM, studies have shown that good glycemic control can prevent peripheral neuropathy. In established diabetic peripheral neuropathy, the evidence is not as good, but some studies show improvement. In hypothyroidism, thyroxine treatment can actually improve the neuropathy.

Answered by: Dr. Ally Prebtani

10. Severe Pruritus in the Elderly

I see elderly patients with severe pruritus, without demonstrable cause. What to do?

Submitted by: Vincent Luykenaar, MD, Coaldale, Alberta

When evaluating pruritus one should determine whether you are dealing with localized or generalized pruritus and whether there are any primary lesions seen. In an elderly patient with generalized pruritus and no primary lesions, the most common cause is xerosis, especially in the winter.

A trial of a topical emollient should be given. If the patient continues to have severe pruritus, then systemic causes of generalized pruritus should be considered. The patient needs to have a full history and physical examination, with attention given to looking for icterus, lymphadenopathy, hepatosplenomegaly, and organomegaly, and the physical examination should include a rectal exam in men and women, and a vaginal exam in women. Laboratory examination should include a CBC, ESR, TSH, LFTs with alkaline phosphatase and bilirubin, serum creatinine, serum ferritin, protein electrophoresis and a chest X-ray. Other investigations will depend on physical findings. If an underlying systemic cause is found, this then needs to be treated, and pruritus should subsequently improve. If no underlying systemic cause can be found, treatment would then consist of emollients and sedating antihistamines to improve symptoms. The patient would also need to be closely followed for the development of signs or symptoms that might suggest an underlying systemic cause. Dx

Answered by: Dr. Richard Haber

Erratum

A recent Experts on Call article, "Describing Incretins" [December 2010, Volume 27, Number 12], has been updated. At the time the response was originally written, no GLP-1 analogues or agonists were available in Canada, as is stated in the response. However, since then, liraglutide has become available; it was approved by Health Canada in May 2010, for the treatment of adults with Type 2 diabetes. It, in addition to the DPP-4 inhibitors, is available to practitioners across Canada. We apologize for any confusion.