1. Carcinoid disease: A review

Please review carcinoid disease.

Submitted by:
A. Mahim, MD
Nasonworth, New Brunswick

Carcinoid syndrome is a consequence of humoral factors produced by carcinoid tumours, including biogenic amines, most commonly serotonin, but may also be associated with the production of polypeptides and prostaglandins. Carcinoid tumours are rare, with the majority located in the gastrointestinal tract (particularly small bowel) or bronchopulmonary system. Symptoms of typical carcinoid syndrome include episodic cutaneous flushing, diarrhea, bronchospasm, telangiectasias and development of cardiac valvular lesions (carcinoid heart disease).

The diagnosis of carcinoid syndrome can be confirmed biochemically by an elevated 24-hour excretion of 5-hydroxyindoleacetic acid, the end product of serotonin metabolism. Once confirmed, the tumour should be localized with a CT scan and, often, radiolabelled octreotide imaging. The majority of patients with carcinoid syndrome have metastatic disease, predominantly in the liver. Management of these patients should include removal of the tumour if localized and treatment of the symptoms of carcinoid syndrome. The somatostatin analogue, octreotide, can be effective in controlling severe symptoms of flushing and diarrhea. Patients with this rare presentation should be referred to oncology and/or surgery for appropriate management.

Answered by:
Dr. Sharlene Gill

2. DRE & PSA between ages 40 and 50

Please comment on DRE and PSA screening in men between the ages of 40 and 50.

Submitted by:
Stephen Miller, MD
Fall River, Nova Scotia

I reserve digital rectal examination (DRE) and prostate specific antigen (PSA) screening for men between 40 and 50 years of age and are at a higher risk of cancer (*i.e.,* family history, black men). I recommend DRE and PSA screening after the age of 50 in men with at least a 10-year life expectency. There are no firm guidelines regarding screening for prostate cancer, since the randomized studies are still ongoing. However, screening identifies earlier-stage cancers compared to non-screened patients. It is unknown if screening reduces overall mortality. Prostate cancer is very low in men under the age of 50.

Answered by:
Dr. Fred Saad

3. Should ICSs be used in COPD?

Should ICSs be used as preventive therapy in COPD patients?

Submitted by:
Hany Kamel, MD
St-Laurent, Quebec

The role of inhaled corticosteroids (ICS) in chronic obstructive pulmonary disease (COPD) remains controversial. Unlike in asthma, ICS are not first-line therapy in COPD. The Canadian Thoracic Society's (CTS) COPD Guidelines state that ICSs have a role in two settings:

1. Treating symptoms of dyspnea and exercise intolerance in individuals who remain disabled despite use of combined inhaled long-acting bronchodilators.
2. Preventing acute exacerbation of COPD (AECOPD) in individuals with severe airflow obstruction (forced expiratory volume in one second < 50% predicted) who continue to experience severe or frequent episodes of AECOPD despite appropriate vaccination, smoking cessation counseling and optimal bronchodilation.[1]

Additional information about COPD management can be obtained from the CTS website at **www.copdguidelines.ca**.

1. O'Donnell DE, Hernandez P, Aaron S, et al. Executive Summary: Canadian Thoracic Society COPD Guidelines: Summary of highlights for family doctors. Can Respir J 2003; 10(4):183-5.

Answered by:
Dr. Paul Hernandez

4. Can ezetral and fenofibrate be given for high fat?

Can you give ezetrol with fenofibrate for high fat?

Submitted by:
D. Rapoport, MD
Downsview, Ontario

The combination of ezetimibe and fibrates has not been studied extensively, but they appear to be effective in the improvement of the lipid profile. More studies are needed with this combination, especially for the high-risk patients that are unable to tolerate statins. At this time, the product monograph does not have an indication for this combination of agents.

Answered by:
Dr. Vincent Woo

5. What's needed for patients with a first degree relative with early heart disease?

Would you offer screening to a person who has a first degree relative with early heart disease? Do these patients need periodic stress tests or homocysteine levels checked or reduced LDL (< 2.6 mmol/L)?

Submitted by:
Gail Dangar, MD
Thornhill, Ontario

Yes. I would perform a history and physical examination and I would also get a fasting lipid profile, assess the risk factor profile and obtain a baseline ECG. If the patient is asymptomatic, I would not do any further diagnostic procedures. Some physicians would consider obtaining an electron beam CT for coronary artery calcification, but the benefit of this strategy has not been definitively demonstrated at this time.

I would not do periodic stress tests, however, I would have a low threshold to do stress testing if they have any symptoms. A routine screening homocysteine is not needed at this time.

Answered by:
Dr. Mark Eisenberg

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6. Can ezetimibe be used as a single lipid-lowering agent?

Can cholesterol absorption inhibitors, such as ezetimibe be used as a single lipid-lowering agent in patients who are allergic/intolerant to all fibrates/statins?

Submitted by:
Jack Kooy, MD
Penticton, British Columbia

Yes. Ezetimibe has not been shown to cross-react in patients intolerant of statins or fibrates. Used as monotherapy, it is less potent than statins. A 10 mg, daily dose, lowers LDL-cholesterol by about 18%, triglycerides by about 8% and increases HDL cholesterol by about 2%, which is significant from placebo.[1] However, patients may also experience side-effects (*i.e.,* gastrointestinal upset, myalgia) from ezetimibe use, though possibly less frequently than from statin or fibrate use.

There are, as yet, no published studies of cardiovascular event reduction benefits with ezetimibe either as monotherapy or in combination therapy.

References
1. Medical Letter 2003; 45(1151):17-9.

Answered by:
Dr. T.K. Lee

7. Oral bisphosphonates & metastatic bone cancer

Is there a role for oral bisphosphonates in metastatic bone cancer?

Submitted by:
Diane Zatelny, MD
Barrie, Ontario

While intravenous bisphosphonates are used more frequently, there is a role for oral bisphosphonates in this setting. Oral clodronate, 1,600 mg, daily, is the most frequently used agent. In randomized controlled trials, clodronate has been shown to reduce pain and mortality, and to lower the number and the risk of new bony metastases in breast cancer patients. Another benefit is the prevention of pathologic fractures. Oral bisphosphonates may also be used for patients with prostate cancer and multiple myeloma.

Answered by:
Dr. Philip Baer

8. What is the best way not to miss a prostate cancer diagnosis?

What is the best way not to miss a prostate cancer diagnosis?

Submitted by:
Raquel Vary, MD
Ville St-Laurent, Quebec

At the present time, there is insufficient evidence to support a single best screening method. Prostate-specific antigen (PSA) is a tumour marker that is being used extensively to screen normal healthy men for prostate cancer. For diagnosis within five years, PSA is reported to have a sensitivity of 65% and specificity of 90%. The initial enthusiasm for PSA screening, however, has been replaced with a more judicious, individualized approach. The challenge is to clinically identify significant cancers at a curable stage and to avoid overdiagnosing indolent, low-grade diseases that would otherwise not compromise one's life expectancy and to minimize the needless anxiety associated with false-positive results.

While there is no direct evidence to support that PSA screening lowers mortality, a suggested approach is to offer it to fit men between the ages of 50 and 70 years, with at least a 10 year life expectancy. Men should be informed of the potential benefits and risks of early detection and should be made aware of the limitations of testing.

Answered by:
Dr. Sharlene Gill

9. Evidence & guidelines for treating pain with IV lidocaine

Is there evidence for treating pain with an infusion of IV lidocaine? Can you offer guidelines for safe use?

Submitted by:
Andy Brockway, MD
Woodstock, Ontario

Intravenous lidocaine has been demonstrated to be effective in certain acute and chronic pain situations, both in animal models and in humans. It has been used mostly in patients with peripheral or central nervous system injuries. There are reports of benefit in patients with chronic fibromyalgia pain as well.

However, this therapy is generally reserved for patients who have failed traditional pain therapies. There is the potential for significant cardiovascular and neurologic events (*i.e.,* arrhythmias and convulsions); therefore, this treatment should only be attempted under vigilant monitoring conditions. It is appropriate to consult a pain specialist if this treatment is considered.

A recent paper by Cahana *et al*, outlines a suggested protocol for use in chronic neuropathic central pain.[1] However, protocols may vary depending on the condition being treated and it is best to consult your local pain centre.

Reference
1. Cahana A, Carota A, Montadon ML, et al: The long-term effect of repeated intravenous lidocaine on central pain and possible correlation in positron emission tomography measurements. Anesth Analg. 2004; 98:1581-4.

Answered by:
Dr. Michael Starr

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10. Retention & untreated BPH

If untreated, what percentage of BPH patients go on to retention?

Submitted by:
John Dawson, MD
Ottawa, Ontario

The overall risk of acute urinary retention is low in men.[1] However, certain factors increase the risk of acute urinary retention, such as:

- Increasing age
- A diagnosis of benign prostatic hyperplasia
- More severe lower urinary tract symptoms, including the sensation of incomplete bladder emptying, having to void again after less than two hours and a weak urinary stream.
- Use of drugs that has effects:
  - on smooth muscle tone (calcium blockers)
  - on the adrenergic nervous system (B-blockers)
  - with anticholinergic effects (antiarrythmics).

References
1. Meigs JB, Barry MJ, Giovannucci E, et al: Incidence rates and risk factors for acute urinary retention: The health professionals followup study. J Urol 1999; 162(2):376-82.

Answered by:
Dr. Fred Saad

11. What to do with a very low HDL?

What should be done about a very low HDL (0.68 mmol/L)? The LDL is 2.0 mmol/L on atorvastatin, 20 mg.

Submitted by:
Wesley Steed, MD
Taber, Alberta

That depends. Exercise and moderate alcohol intake can increase a low HDL. I would not initiate medical therapy for a low HDL for primary prevention unless the patient has multiple risk factors. If the patient has multiple risk factors, niacin can be added to increase the HDL. For secondary prevention (*e.g.,* post-MI, post-percutaneous coronary intervention, post-coronary artery bypass graft), I would initiate therapy with niacin in addition to the atorvastatin, which the patient is already taking.

Answered by:
Dr. Mark Eisenberg

12. How do I determine if a patient needs to carry an epinephrine injection?

How do I determine whether a patient needs to carry an epinephrine injection?

Submitted by:
Justin Lou, MD
Toronto, Ontario

Single dose units of epinephrine (0.5 mg or 0.3 mg) are often prescribed for individuals with various food and insect sting allergies. More important than the actual allergy in question is the history of the patient's reaction. Did the patient develop a systemic acute event, which may have included respiratory, gastrointestinal, neurologic or cardiovascular symptoms? In all these cases, including idiopathic and exercise induced anaphylaxis, epinephrine is indicated, as well as instruction to avoid the precipitating cause. If a patient develops acute urticaria that lasts several days or weeks, with no known underlying trigger, the cause is often presumed to be infectious in origin and an EpiPen® is not required.

There are certain food allergies that, when diagnosed, would automatically indicate the need for an EpiPen®. These include peanut, nut, fish, seafood and, more recently, seed allergy. Almost all children with egg and milk allergies require an Epipen®, unless the sole manifestation of the allergy is a delayed exacerbation of their underlying eczema.

Other conditions that would necessitate an EpiPen® prescription:

- Venom allergy
- Patients with cold-induced urticaria
- Severe asthmatics with a history of acute reactions to horse dander

Provision of more than one injector is often recommended, since a second dose may be needed prior to arrival at a medical facility. A new device, Twinject™, is now available and includes a second dose. More teaching is required with the use of the second dose and this device may not be suitable for everyone.

Answered by:
Dr. Tom Gerstner

13. Approaching a chronic cough problem

What is the best approach to a chronic cough problem?

Submitted by:
Jack Leung, MD
Vancouver, British Columbia

Chronic cough (lasting > eight weeks) is an extremely common presenting complaint in the primary-care setting.

Recently published, evidence-based clinical practice guidelines report that the most common causes of chronic cough in adult non-smokers with a normal chest roentgenogram that are not taking an angiotensin converting enzyme inhibitor include, upper airway cough syndrome (formerly called post-nasal drip syndrome) due to various rhinosinus conditions, asthma, gastroesophageal reflux disorder and nonasthmatic eosinophilic bronchitis.[1] For each of these conditions, cough may be the only symptom. A focused approach to investigation and treatment of these four conditions is likely to result in a successful outcome in the majority of patients with chronic cough. Failure for cough to resolve with this management approach warrants referral to a cough specialist.

Additional information from the American College of Chest Physicians can be found at **www.chestjournal.org**.

References
1. Irwin RS, Baumann MH, Bolser DC et al: Diagnosis and management of cough: ACCP evidence-based clinical practice guidelines. CHEST 2006; 129(1 Suppl):1S-292S.

Answered by:
Dr. Paul Hernandez

14. Treating mild asthma in young adults

Is montelukast recommended besides albuterol +/- corticosteroids, as required, in the treatment of mild asthma in young adults?

Submitted by:
David Grunbaum, MD
Lachine, Quebec

As needed use of leukotriene receptor antagonists (LTRA) is generally not recommended, due to slow inset of action. For asthma, a clinical benefit requires from one to several days of therapy and in one study of allergic rhinitis, it took two days for LTRA benefits to start and two weeks for maximum effect. In exertion-induced bronchoconstriction, no effect was seen at two hours; a small effect was seen at 12 hours; and no benefit was seen at 24 hours following a single dose of montelukast.

Answered by:
Dr. Rick Hodder

15. Chromium supplementation & Type 2 diabetes

Do you recommend chromium supplementation for Type 2 diabetes patients?

Submitted by:
Michelle Sue, MD
Toronto, Ontario

Numerous case reports and small limited studies have shown the effectiveness of chromium supplementation in patients with diabetes. Some of these studies have shown a lower fasting glucose level, improved lipid profile and hemoglobin A1c lowering. Large, well controlled studies are needed to clarify the effectiveness of chromium in diabetes. Chromium appears to be safe except, possibly, in very high doses. At this time, it cannot be recommended for use due to the lack of good clinical trials.

Answered by:
Dr. Vincent Woo

16. Are probiotics created equal?

Are probiotics created equal?

Submitted by:
JR Gray, MD
Vancouver,
British Columbia

One of the most widely studied and utilized probiotics is VSL#3. This probiotic has demonstrated clear efficacy in pouchitis, improves symptom in patients with irritable bowel syndrome (IBS) and randomized, placebo-controlled trials are currently underway to evaluate the efficacy of VSL#3 in patients with active ulcerative colitis.

Several studies have been conducted evaluating the efficacy of various probiotic combinations in alleviating the symptoms of IBS. One probiotic mixture has demonstrated a median reduction of 42% in symptoms in the probiotic group versus 6% in the placebo group. Another study showed that VSL#3 reduces flatulence scores and retards colonic transit without altering bowel function in patients with IBS and bloating. Other studies have yielded conflicting results. A double blind, placebo-controlled, six-month trial, did not show improvements with a probiotic treatment containing *lactobacillus reuteri*. Overall, the current data suggests an overall improvement in IBS symptoms in patients treated with probiotics.

However, as this field of therapeutics is in its infancy, the underlying mechanisms of action and indications for use remain to be clarified. Furthermore, there is a wide variety of preparations available on the market today, which contain any assortment or combination of live microbial organisms. However, many commercially available probiotic formulations have shown inconsistent results with respect to bacterial viability and identity. VSL#3 is one of a very few preparations with demonstrated quality control and safety profile. Given that each organism exerts a specific effect through a unique mechanism, and that there are no strict guidelines governing the use of these agents, it is no surprise that there are no large randomized, placebo-controlled trials comparing one probiotic preparation vs. another in a head-to-head fashion. Therefore, there is no evidence that demonstrates superior efficacy or cost-effectiveness of any probiotic. Dx

Answered by:
Dr. Robet Bailey
Dr. Denny Demeria