1. Elevated homocysteine levels

What would you prescribe for someone with elevated homocysteine levels?

Submitted by:
Pat Cunningham, MD
Brantford, Ontario

There is reasonably good evidence from population studies that elevated homocysteine levels are associated with an increased risk of cardiovascular disease. Vitamins, such as B12, B6 and folate, are involved in homocysteine metabolism and supplementation has been shown to reduce homocysteine levels. Typical combinations include 2 mg of folate, 500 mg B12 and 100 mg B6 daily.

Although one study of lowering homocysteine post-angioplasty showed a reduction in restenosis, another trial demonstrated an increased restenosis rate. The Vitamin Intervention for Stroke Prevention (VISP) trial demonstrated that lowering homocysteine in stroke survivors did not reduce the composite endpoint of stroke (*i.e.*, coronary heart disease or death).[1] The Heart Outcomes Prevention Evaluation (HOPE-2) investigators studied patients with stable disease and those at high vascular risk, while the Norwegian Vitamin Trial (NORVIT) trial studied patients with seven days post-myocardial infarction (MI).[2-3]

Both studies demonstrated significant reductions in homocysteine levels, with vitamin treatment, but failed to demonstrate a reduction in MI, stroke or cardiovascular death.

Based on the evidence from these large randomized clinical trials, there is no role for treatment of elevated homocysteine with B12, B6 or folate.

References
1. Toole JF, Malinow R, Chambless LE, et al: Lowering homocysteine in patients with ischemic stroke to prevent recurrent stroke, myocardial infarcation, and death: The Vitamin Intervention for Stroke Prevention (VISP) randomized controlled trial. JAMA 2004; 291(5):565-75.
2. The Heart Outcomes Prevention Evaluation (HOPE) 2 Investigators: Homocysteine Lowering with folic acid and B vitamins in vascular disease. NEJM 2006; 354(15):1567-77.
3. NORVIT Trial Investigators: Homocysteine lowering and cardiovascular events after acute myocardial infarction. NEJM 2006; 354(15):1578-88.

Answered by:
Dr. Kenneth Gin

2. Choosing the right statin

How should statins be chosen for different total cholesterol, LDL, HDL and TG levels?

Submitted by:
W.A.C. MacDonald, MD
Petrolia, Ontario

In combined dyslipidemias the most frequent pattern is low HDL-cholesterol and high triglyceride level. The effect of statins on raising the levels of HDL-cholesterol is minor, between three per cent to 10% and there are no clinically meaningful differences between the various statins. Although there are differences in the effect of different statins on the triglyceride levels, the need to primarily address the HDL-cholesterol levels usually calls for a combination of statins with fibrates or niacin.

Answered by:
Dr. George Fodor

3. Breast cancer screening

What is the recommended screening for women < 40 years of age with a strong family history of breast cancer?

Submitted by:
Nav Gill, MD
Surrey, British Columbia

Women may be encouraged to do regular breast self-examinations, usually to be performed in the week following a menstrual period, as well as part of their annual physical examination.

Screening mammography is recommended for women between 40 and 79 years of age. However, family physicians may wish to refer women under 40 years of age with a strong family history of breast cancer—defined as two or more first-degree relatives with premenopausal breast cancer—for screening. Such women should also be considered for genetic counselling and assessment for hereditary cancer.

The use of diagnostic mammography and ultrasound may be useful as part of the diagnostic workup of a breast mass. However in the absence of an abnormality on mammography or physical exam, an ultrasound is not required for screening.

References
1. Screening Mammography Program of British Columbia guidelines. British Columbia Health Ministry, 2005.

Answered by:
Dr. Sharlene Gill

4. Diagnosing diabetes mellitus in the pediatric population

How do you diagnose diabetes mellitus in the pediatric population? Are the lab investigations and values the same as in adults?

Submitted by:
Sakina Raj, MD
Calgary, Alberta

The diagnosis of diabetes in the pediatric population is made in the same manner as in the adult population.

Type 2 diabetes is increasing in prevalence in children, especially in high-risk populations. The diagnosis of diabetes is made:

- if the fasting plasma glucose is > 7.0 mmol/L,
- when the casual plasma glucose is > 11.1 mmol/L with typical signs and symptoms of diabetes, or
- after a 75 g oral glucose tolerance test with a two-hour plasma glucose level > 11.1 mmol/L.

If the individual is metabolically stable, a confirmatory test is required on a second day.

Answered by:
Dr. Vincent Woo

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5. Antibiotic choices for COPD patients

? What is the best antibiotic choice in a COPD patient that develops an acute exacerbation of community-acquired pneumonia? Is there reason to be concerned about long QTc interval with certain antibiotic choices?

Submitted by:
Karen Arnold, MD
North Vancouver, British Columbia

There is evidence of the benefit of antibiotic use to treat chronic obstructive pulmonary disease (COPD) with acute exacerbation (AECOPD) in individuals who experience increased dyspnea associated with a change in sputum volume and/or purulence. The Canadian Thoracic Society recommends that first-line antibiotic therapy be chosen on the basis of risk factors for treatment failure (*i.e.*, forced expiratory volume in the first second of exhalation < 50% predicted, frequent exacerbations, recent treatment with an antibiotic for AECOPD, ischemic heart disease, or use of home oxygen).[1] For those without risk factors, patients can be treated with trimethaprim/sulfamethoxazole, amoxicillin, doxycycline, second generation cephalosporin, or an extended spectrum macrolide. Patients with risk factors should be treated with either amoxicillin/clavulanate, or a fluoroquinolone.

Recommended empiric antibiotics to treat outpatient community-acquired pneumonia in patients with COPD that have not recently received antibiotic therapy includes an extended spectrum macrolide or doxycycline.[2] COPD patients that have recently received an antibiotic should be treated with a respiratory fluoroquinolone or the combination of amoxicillin/clavulanate or second generation cephalosporin and a macrolide.[2]

Prolongation of QT interval, which is associated with serious life-threatening ventricular arrhythmias (*e.g.*, *torsades de pointes*), has been reported with both fluoroquinolones and macrolides. These antibiotic classes should be avoided or only used with extreme caution in patients with prolonged QT or in those patients with other risk factors for prolonged QT (*e.g.*, hypokalemia, hypomagnesemia, or concomitant use of other drugs that can prolong QT).

References
1. O'Donnell DE, Hernandez P, Aaron S, et al: Canadian Thoracic Society COPD Guidelines: Summary of highlights for family doctors. Can Respir J 2003; 10(4):183-5.
2. Mandell LA, Marrie TJ, Grossman RF, et al: Summary of the Canadian guidelines for initial management of community-acquired pneumonia: An evidence-based update by the Canadian Infectious Disease Society and the Canadian Thoracic Society. Can J Infect Dis 2000; 11(5): 237-48.

Answered by:
Dr. Paul Hernandez

6. Virtual colonoscopy

What is the current state of the art in virtual colonoscopy for detecting colon cancer?

Submitted by:
W. Taylor, MD
Medicine Hat, Alberta

Virtual colonoscopy (VC), also known as computed tomography colonography, utilizes images acquired by conventional computed tomography to generate computer-reconstructed two-dimentional and three-dimensional images of both the colon and rectum. While minimally invasive, it does require bowel preparation, cleansing and gas insufflation.

Several studies have evaluated the performance of VC as a screening tool for colorectal polyps and cancer. In a meta-analysis of 33 studies (n = 6393)[1], VC—when compared to a reference standard of optical colonoscopy—had a pooled specificity of 86% (84% to 88%) and low to moderate sensitivity of 70% (53% to 87%). Test characteristics improved as polyp size increased. The heterogeneity in sensitivity is most likely related to variability in scanning and reconstruction technology, radiologist experience and patient risk status.

Although promising, it is not yet suitable as a tool for mass screening until its performance can be standardized and cost-effectiveness can be predicted. In the meantime, it may be a reasonable consideration for patients unable to tolerate a colonoscopy due to risk factors, technical difficulty, or obstruction.

References
1. Mulhall B, Veerappan G, Jackson J: Meta-Analysis: Computed Tomographic Colonography. Ann Intern Med 2005; 142(8): 635-50.

Answered by:
Dr. Sharlene Gill

7. Increased pneumonia risk with long-term PPI treatment?

Should I be concerned about the increased risk of pneumonia in patients on long-term PPIs?

Submitted by:
Mohamed I. Ravalia, MD
Twillingate, Newfoundland

(For more info on PPI use, go to page 75)

A number of theoretical concerns have been raised about the effects of long-term gastric acid suppression since the introduction of proton pump inhibitor (PPI) agents, including:

- masking or development of upper gastrointestinal (UGI) malignancy,
- malabsorption of nutrients and
- pathogen colonization of the UGI tract.

To date, despite widespread use of PPIs, none of these concerns have been realized in clinical practice. A recent retrospective, case-controlled, cohort study from a large population database from the Netherlands assessed the risk of community-acquired pneumonia (CAP) with gastric acid suppression.[1] The authors concluded that current PPI users had a 1.89-fold increase in the relative risk of developing CAP compared to individuals who stopped PPI treatment. This translates into approximately one extra case of pneumonia for every 100 years of patient exposure to PPI.

A major criticism of this study is that individuals who require ongoing PPI use likely have more severe UGI problems, such as gastroesophageal reflux, which itself is associated with increased risk of pneumonia. Therefore, until a placebo-controlled, prospective trial of PPI is conducted with CAP as the primary outcome, there will be no definitive answer to this question. No medication is without risk of adverse effects; the possibility of a very small risk for CAP with long-term PPI use must be balanced against the benefit of treatment of the condition for which PPI is prescribed.

References
1. Laheij RJ, Sturkenboom MC, Hassing RJ, et al: Risk of community-acquired pneumonia and use of gastric acid-suppressive drugs. JAMA 2004; 292(16):1955-60.

Answered by:
Dr. Paul Hernandez

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8. Antidepressants for teenage patients

With all the concern in the media on the use of antidepressants in teenagers, which medication is the best choice for a clearly depressed teenager?

Submitted by:
Dennis Glubish, MD
St. Albert, Alberta

Before prescribing an antidepressant for an adolescent with depression, carefully screen them to rule out bipolar disorder.

Psychoeducation and manual-based psychotherapeutic approaches (*i.e.*, cognitive behavioural therapy) should be considered first. If antidepressants are to be prescribed, consult the recently published Canadian Psychiatric Association and the Canadian Network for Mood and Anxiety Treatments position statement on this topic. Patients and their families should be informed of all risks vs. benefits.

Fluxoxetine is the only antidepressant with compelling evidence. Other antidepressants and adjuvant strategies need to be considered on a case by case basis, carefully evaluating the therapeutic index of each approach.

References
1. Canadian Psychiatric Association and the Canadian Network for Mood and Anxiety Treatments (CANMAT): Clinical guidelines for the treatment of depressive disorders. Can J Psychiatry 2001; 46(Suppl 1): 1-91S.

Answered by:
Dr. Roger S. McIntyre

9. Tamoxifen: suitable for breast cancer prophylaxis in high-risk patients?

? What is the indication for tamoxifen in preventive treatment of a close family member (sister) of a breast cancer patient?

Submitted by:
Michel Lauzon, MD
Deux-Montagnes, Québec

Primary prevention for the development of breast cancer is an active area of investigation. However, to date, there is insufficient evidence in support of a recommendation for tamoxifen in this setting.

Four large studies have reported conflicting results on the role of tamoxifen in primary prevention among women at increased risk of developing breast cancer. The two larger trials reported a small, but statistically significant, decrease in the absolute risk of estrogen receptor positive (but not estrogen receptor negative) breast cancer, while the other two studies demonstrated similar numbers of both subtypes in both the tamoxifen and the placebo arms. These studies have yet to demonstrate either an increase in overall survival or reduction in breast cancer-related mortality, nor have they addressed the questions of optimal duration of therapy or optimal timing for instituting therapy.

Furthermore, tamoxifen is associated with serious adverse events, including endometrial cancer and thromboembolic events. Until more evidence on primary prevention becomes available, timely screening (as outlined by local screening guidelines) and consideration of genetic counselling remain the most appropriate interventions for young women with a compelling personal or family history of breast cancer.

Answered by:
Dr. Heather McArthur
Dr. Sharlene Gill

10. Corticosteroid inhalers for COPD prophylaxis?

Should corticosteroid inhalers be used as preventative therapy in COPD patients?

Submitted by:
Hany Kamel, MD
Montreal, Quebec

I reserve regular inhaled corticosteroids (ICS) for patients with advanced chronic obstructive pulmonary disease (COPD) (*i.e.*, whose forced expiratory volume in the first second of exhalation < 50% predicted). These patients, as opposed to those with a milder form of the disease, are likely to have about 25% fewer COPD exacerbations in response to ICS.

I also use ICS for patients with both COPD and asthma (about 10% to 15% of clinical COPD patients). You can identify these mixed patients if they have:

- significant allergies,
- very twitchy airways and
- if they quickly feel a lot better after a couple puffs of salbutamol.

Answered by:
Dr. Rick Hodder

11. Differentiating PsA from RA

How do I differentiate PsA from RA ?

Submitted by:
Daryl Bain, MD
Timmins, Ontario

This can be a challenge, since psoriatic arthritis (PsA) can mimic the symptoms of rheumatoid arthritis (RA) and has similar potential to cause destructive and disabling arthopathy.However, in PsA, the psoriasis usually precedes the arthritis (vice-versa in only about 15%) and rheumatoid factor is not found in the serum of PsA patients.

Also, PsA can have a variety of joint presentations that are different than typical RA. For example, PsA may present as an asymmetric oligoarthritis, distal interphalangeal joint involvement in the hands, sacroiliitis, or dactylitis (sausage digit). These would not be typical features for RA.

Radiographically, the erosions of PsA are different than those seen in RA and this can also help to distinguish between these conditions. However, the basic approach to treatment is similar in that we now move quickly to use disease-modifying drugs and the newer biologic agents, which also play an important role in preventing joint destruction and maintaining function.

Answered by:
Dr. Michael Starr

Cont'd on page 36 →

12. Osteopenia treatment

How do I treat moderate osteopenia in the post-menopausal woman with no positive family history of osteoporosis? What about the premenopausal woman?

Submitted by:
Gayle Garber, MD
Conception Bay South, Newfoundland

In 1994, the World Health Organization published definitions of osteoporosis and osteopenia based on the reported T-scores of bone densitometry testing. These definitions were appealing as they were simple and unitless. However, it is now clear that bone mineral density (BMD) is only one of several factors that contribute to a patient's risk of fracture.

The latest Osteoporosis Society of Canada guidelines have suggested that BMD reports include a 10-year fracture risk to aid the clinician in determining the need for therapy. There are a number of clinical factors that contribute to this fracture risk calculation. Age is the first variable that must be considered, since fracture risk increases with age, regardless of BMD. There are other clinical factors that may move a patient into a higher risk category. The most important are a previous history of a fragility fracture (after age 40) and the systemic use of glucocorticoids for more than three months.

Table 1 illustrates that a young woman with osteoporosis may be only at moderate risk, whereas an 80-year-old with osteopenia may be at high risk for fracture.

The presence of any high risk feature, such as glucocorticoid use, increases risk categorization to the next level (*i.e.*, moderate category becomes high-risk category). Although all patients require adequate calcium, vitamin D and exercise, this new method of reporting helps the clinician to decide which patients may benefit from further therapy. It also reinforces the idea that most premenopausal women would be satisfactorily treated with adequate calcium and vitamin D alone. Dx

Table 1.

Fracture Risk in Women

	10-year risk factor		
Age	Low < 10%	Moderate 10% to 20 %	High > 20%
50	> -2.3	-2.2 to -3.9	< -3.9
55	> -1.9	-1.9 to -3.4	< -3.4
60	> -1.4	-1.4 to -3.0	< -3.0
65	> -1.0	-1.0 to -2.6	<-2.6
70	> -0.8	-0.8 to -2.2	< -2.2
75	> -0.7	-0.7 to 2.1	< -2.1
80	> -0.6	-0.6 to -2.0	< -2.0
85	> -0.7	-0.7 to -2.2	< -2.2

Answered by:
Dr. Michael Starr
Dr. Elizabeth Hazel