



Answers to your questions
from our medical experts

1. Choosing a PPI



Is there a clinically significant difference between the available PPIs?

Submitted by:
Murray Stanwood, MD
Victoria, British Columbia

A number of proton pump inhibitors (PPIs) are available on the market to treat acid-related gastrointestinal disorders (Table 1). Although they vary in molecular structure, dosage, cost and metabolism, there is *no* clinically significant difference between them.

Table 1

Comparison of available proton pump inhibitors

Pharmacologic name	Dosage	Cost/dose
• Esomeprazole	• 40 mg q.d.	• \$2.21
• Lansoprazole	• 30 mg q.d.	• \$2.10
• Omeprazole	• 20 mg q.d.	• \$2.31
• Pantoprazole	• 40 mg q.d.	• \$1.99
• Rabeprazole	• 20 mg q.d.	• \$1.36 (\$0.68/10 mg)

If given sufficient doses regularly, PPIs can reduce daily gastric acid secretion by > 95%. All PPIs bind to a common, distinct site on the sub-unit A of the proton pump in the parietal cells.¹

Many studies have compared the various PPIs to each other and they have shown similar potency and efficacy in treating various acid-peptic disorders.²⁻⁶ The side-effects of PPIs are minimal, but for reasons unknown to us, some patients seem to respond and tolerate certain PPIs better than others.

In summary, all five currently available PPIs have similar efficacy. The decision as to which PPI to use needs to be individualized based on patient response, as well as on cost. Newer PPIs, such as sublingual and continuous-release formulations, are in development.

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Answered by:
Dr. Robert Bailey

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2. Penicillin allergy from amoxicillin treatment?

What is the best treatment for mononucleosis? Does treatment with amoxicillin cause a penicillin allergy?

Submitted by:
Gordon Milne, MD
Thunder Bay, Ontario

Mononucleosis, a common viral illness, has often been unnecessarily treated with amoxicillin. It was observed long ago that in the presence of this Epstein-Barr virus (EBV), treatment with a penicillin often resulted in a diffused, delayed maculopapular erythematous eruption, lasting for several days. This eruption is not unlike a typical viral exanthem, but its presence in this setting occurred so frequently that it has been said—perhaps somewhat tongue-in-cheek—that administering amoxicillin in a suspected case of mono may be a useful diagnostic tool!

EBV is not unique in its ability to increase the frequency of these types of rashes during penicillin treatment. Needless to say, this is not an IgE-mediated process and therefore the diagnostic and predictive values of skin tests are low, as maculopapular skin rashes occurring during amoxicillin administration are often attributable to infectious diseases, interactions between the drug and infectious agents, or other immunologic mechanisms.

Answered by:
Dr. Tom Gerstner

3. Diagnosing diabetes

What laboratory tests are now recommended in the diagnosis of diabetes mellitus?

Submitted by:
Branislav Belovic, MD
Belleville, Ontario

The diagnosis of diabetes is made by one of three ways:

1. A fasting (*i.e.*, no caloric intake for at least eight hours) plasma glucose > 7.0 mmol/L
2. Casual plasma glucose > 11.1 mmol/L and symptoms of diabetes
3. Two-hour plasma glucose in a 75 g oral glucose tolerance test > 11.1 mmol/L

In the absence of unequivocal hyperglycemia, a confirmatory laboratory glucose test must be done in all cases on another day, accompanied by acute metabolic decompensation.

Answered by:
Dr. Vincent Woo

4. Role of amantadine in upper respiratory tract infections



What is the role of amantadine to decrease the likelihood of an upper respiratory tract infection?

Submitted by:
A. Sood, MD
Toronto, Ontario

Amantadine hydrochloride is an antiviral medication that interferes with Influenza A virus replication, but is ineffective against other respiratory viruses, including Influenza B. Pending susceptibility testing, amantadine is not recommended by the Public Health Agency of Canada for influenza prophylaxis in the 2006 to 2007 season, due to high rates of resistance during the last influenza season.¹ Instead, the neuraminidase inhibitor oseltamivir is approved for prophylaxis against Influenza A and Influenza B.

Antiviral medications should not replace annual influenza vaccinations; however, during seasons in which Influenza A isolates are susceptible to amantadine, there are certain settings in which these medications may be indicated. Indications include:

- helping control influenza outbreaks among high-risk residents of institutions
- for prophylaxis when influenza vaccines are unavailable, contraindicated or administered late and
- for prophylaxis in unvaccinated close contacts of individuals infected with Influenza A.


Individuals taking amantadine should be carefully monitored for side-effects and drug interactions, particularly the elderly or individuals with renal impairment, liver disease, seizure or psychiatric disorders.

References

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Answered by:

Dr. Paul Hernandez






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5. Duration of treatment for a panic disorder

? How long do you continue pharmacotherapy for a panic disorder? Patients frequently experience a relapse of symptoms when they taper the dose (often done on their own). Are they having withdrawal symptoms, or are they still suffering from their disorder? How do we distinguish one from the other?

Submitted by:
Stuart Glaser, MD
 Town of Mount Royal, Quebec

The duration of pharmacotherapy for a panic disorder varies from patient to patient and depends on whether the panic disorder was triggered by an adverse event (e.g., following a serious car accident), or due to a genetic predisposition. In the latter case, there would be a positive family history for anxiety disorders and the patient might develop the panic disorder sometime in adolescence or early adulthood without any triggering traumatic events. If triggered by an adverse event, the duration of pharmacotherapy would be limited to somewhere between six months and one year, provided the patient gets concomitant supportive counselling. In a situation where the patient has a genetic predisposition to anxiety disorders, the pharmacotherapy will be long-term, perhaps for many years. Of course, each case should be considered individually.


There is a difference between the symptoms of the underlying condition and the symptoms of withdrawal. Withdrawal symptoms usually occur when the medication is stopped abruptly, are usually acute and along with feelings of panic and anxiety, include physical manifestations, such as:

- palpitations,
- excessive sweating,
- shakiness and
- sometimes, some GI symptoms.

Patients usually describe these symptoms as different from their regular panic attacks.

On the other hand, when the medication dosage is gradually reduced, the patient may experience a gradual resurgence of the initial panic attacks for which they were prescribed the medication in the first place. In this case, the symptoms reappear gradually and get worse with further tapering of the medication dosage. It is unusual that a gradual reduction of the medication dosage would cause true withdrawal symptoms.

Answered by:
Dr. Hany Bissada

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6. Is allergy and asthma incidence increasing?



Why is allergy and asthma increasing in prevalence?

Submitted by:
Joseph Butchey, MD
London, Ontario

The answer to this perplexing question continues to elude researchers worldwide. At this point, the simple answer would be: we don't know, despite the fact that a great deal of evidence has been amassed to support various theories.

Probably, the most important theory in recent years—for which there is substantial evidence—is the so-called “hygiene hypothesis,” first put forward by Strachan in 1989.¹ This theory states that the overly-hygienic Western lifestyle results in less infectious illnesses early in life, which then allows the “unstimulated” immune system to start reacting to innocuous stimuli (e.g., pollen), resulting in the phenotype of various allergic diseases. The reduced incidence of allergy in developing and poor countries and an increase in prevalence in countries that have adopted a more Western lifestyle (e.g., increased atopic disease prevalence in East Germany, after reunification) would support this hypothesis. A lower incidence of allergic disease in larger families and in children who attend daycare (who have had more frequent infectious illness in the first two to three years of life) would also be consistent with this theory. In some populations, exposure to endotoxin (bacterial cell wall component), farm animals and pets early in life has also been shown to reduce onset of subsequent allergic disease.

However, many questions remain unanswered and as these relationships are looked at more carefully, it seems there is likely a strong gene-environmental interaction (*i.e.*, different exposures resulting in different outcomes, depending on the underlying genotype). It must also be noted that, at least part of the observed increase in the prevalence of asthma and allergic disease may be related to increased recognition in recent years and in some cases, perhaps leading to over-diagnosis of asthma.

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Answered by:
Dr. Tom Gerstner

7. Investigating asymptomatic high BP

What is recommended as the basic investigation for asymptomatic high BP patients without any clinical risk factors? Is the ECG still valuable?

Submitted by:
Michel Broudlet, MD
Montreal, Quebec

In the event that a high BP is measured in an otherwise asymptomatic patient, an additional two readings should be measured during the same visit. I would then proceed with a review of the patient's history, searching particularly for target organ damage, such as evidence of:

- coronary disease,
- cerebrovascular disease,
- peripheral arterial disease or
- renal insufficiency.

At the second visit, if the BP remains elevated, further history and physical examination should be performed, as well as the following diagnostic tests:

- urinalysis,
- complete blood count,
- blood chemistry,
- fasting glucose,
- lipid profile and
- a standard 12-lead ECG.

By the third visit, in the absence of target organ damage and/or increased cardiovascular risk, if systolic BP is > 160 mmHg and/or diastolic BP is > 100 mmHg, the patient can be diagnosed as having hypertension. If at the third visit, systolic BP is 140 mmHg to 159 mmHg and/or diastolic BP is 90 mmHg to 99 mmHg, up to two to three further visits may be required to properly diagnose hypertension.

With regards to the issue of the value of an ECG in this case, as a general rule, if BP remains elevated after two visits, a 12-lead ECG should be requested to assess for the presence of left ventricular hypertrophy (LVH)—an indicator of target organ damage. It should be noted that, while an ECG can provide a highly specific diagnosis of LVH, an ECG's sensitivity for detecting LVH is low. This is important because it facilitates the identification of patients with less favorable prognosis and lowers the threshold for which pharmacologic therapy would be initiated (*i.e.*, Grade 1 hypertension = systolic BP of 140 mmHg to 159 mmHg and/or diastolic BP of 90 mmHg to 99 mmHg).

Answered by:
Dr. Igal A. Sebag

8.

Clopidogrel: a universal diabetes treatment?



Should all diabetes patients be on clopidogrel?

Submitted by:
Greg Baran, MD
Kingston, Ontario

No. At this time, there is no evidence at this time suggesting that all individuals with diabetes should be on clopidogrel. In Canada, clopidogrel is indicated for the secondary prevention of atherothrombotic events in patients with atherosclerosis documented by stroke, MI, or established peripheral arterial disease, such as:

- MI,
- ischemic stroke,
- cardiovascular death and/or
- refractory ischemia.

Clopidogrel in combination with acetylsalicylic acid is indicated for the early and long-term secondary prevention of atherothrombotic events in patients with acute coronary syndromes without ST-segment elevation.

Answered by:
Dr. Vincent Woo

9.

Anxiety disorder medication and pregnancy



A 28-year-old woman with an anxiety disorder, who has taken 25 mg of sertraline hydrochloride q.d. for the past seven years, wishes to become pregnant. Should we have any concern for her and her potential fetus?

Submitted by:
Stephen Coyle, MD
Winnipeg, Manitoba

Sertraline hydrochloride at 25 mg q.d. is a very small dose and stopping it should not usually result in any serious withdrawal effects. Sertraline hydrochloride doesn't have active metabolites and it is considered to be one of the safest among all selective serotonin reuptake inhibitors (SSRIs) for pregnancy. However, safety here is relative to other SSRIs and is certainly not absolute. My opinion is that the anxiety disorder that responded to such a low dose is not severe enough to justify the risk of complications during pregnancy—small though it may be.

The studies available are not conclusive, as they are mainly animal studies, since it is practically impossible to conduct the required research on prescribing SSRIs to pregnant women. My advice is, unless it is absolutely necessary to treat a pregnant woman with an SSRI (*i.e.*, to prevent serious suicide risk due to depression), I would strongly advocate against prescribing any anti-depressant medication for a pregnant woman with a mild-to-moderate anxiety disorder.

Answered by:
Dr. Hany Bissada

10. Prostatic massage: a how-to

? Is prostatic massage—to determine infectious chronic prostatitis by culturing the initial stream—a common procedure? How do you prepare the patient to avoid embarrassment to both parties? (I have never done this, nor have any of my urology consultants).


Submitted by:
Trevor Gin, MD
Delta, British Columbia

The minimum examination required for a patient being assessed for a chronic prostatitis syndrome is a prostate examination. Prior to the prostate examination, a midstream urine should be collected for culture (a pre-prostatic massage urine specimen).

The prostate examination should follow a careful examination of the abdomen and external genitalia. It is easiest to then have the patient roll into the lateral decubitus position (on his side, on the examination table, with knees pulled toward his chest) and perform a gentle, careful prostate examination to rule out clinically detectable prostate cancer nodules. Assess the size and any tender areas in the prostate, the lateral side walls and the floor of the pelvis, as well as the perineum. The patient should then be told that you will be conducting a massage to "squeeze" out prostate secretions or fluid. The patient must be told that it is uncomfortable, but it will only take 15 seconds to 30 seconds. Start at the edge of the base of the prostate (furthest in) and roll your finger tip firmly from lateral to medial. Do this in the mid area of the prostate and at the apex (the area closest to the anus). Repeat the procedure on the other side. When the patient is able, have him void the first 10 cc to 15 cc of urine (this will pick up the fluid that was "milked" into the prostatic urethra) into a sterile container for culture.

If bacteria is growing in the second specimen (post-massage sample) and not the first (pre-massage sample) or in higher numbers in the post-massage urine sample, the patient is diagnosed with chronic bacterial prostatitis. If the cultures are negative, the patient has chronic non-bacterial prostatitis or chronic pelvic pain syndrome.

Answered by:
Dr. J. Curtis Nickel



Ciprallex® (escitalopram oxalate) is indicated for the symptomatic relief of Major Depressive Disorder (MDD). The effectiveness of Ciprallex in long-term use (i.e. more than 8 weeks) has not been systematically evaluated in controlled clinical trials. Ciprallex is not indicated for use in children under 18 years of age. Rigorous clinical monitoring for suicidal ideation or other indicators of potential suicidal behavior is advised in patients of all ages. This includes monitoring for agitation-type emotional and behavioral changes. Please refer to accompanying prescribing information for full dosing instructions and other important information. Product Monograph available on request. ©Registered trademark of Lundbeck Canada Inc. PAAB

11. Pneumococcal vaccine for all diabetics?



Is there any role for pneumococcal vaccines in otherwise healthy diabetics?

Submitted by:
Diane Zatelny, MD
Barrie, Ontario

The pneumococcal immunization of adults with diabetes is encouraged, although there are few studies evaluating its use in this population. The 2003 Canadian Diabetes Association clinical practice guidelines recommend its use, as well as a one-time revaccination for individuals aged > 65 years, if either:

- more than five years had passed since their last vaccination or
- they were < 65-years-old when last vaccinated.

Other indications for revaccination that may be relevant for patients with diabetes include:

- nephrotic syndrome,
- chronic renal disease and
- other immunocompromised states, such as post-organ transplantaion.

Answered by:
Dr. Vincent Woo

12. Role of magnesium sulfate in acute asthma management



What is the role of magnesium sulfate in acute asthma management?

Submitted by:
Bernard Seguin, MD
Clarence Creek, Ontario

Asthma exacerbations can range in severity from mild, self-limited to life-threatening events. Recently, a number of studies have been published evaluating the efficacy of magnesium sulfate (MgSO₄) in the treatment of asthma exacerbations. MgSO₄ can be administered acutely, either intravenously or nebulised for inhalation. Magnesium is a predominantly intracellular cation, dependent on dietary intake for maintenance of homeostasis.

Administration of MgSO₄ results in smooth muscle relaxation and bronchodilation. Current evidence in adults and children suggests that MgSO₄ may provide additional benefit to standard treatment with inhaled β-agonist and systemic corticosteroid medications, particularly in the setting of severe acute asthma exacerbations. The benefits reported are in respect to the degree of improvement in lung function and possibly in the rates of hospitalization. Further studies are needed to clarify benefits of MgSO₄ in asthma exacerbations for other clinically meaningful outcomes.

References

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Answered by:
Dr. Paul Hernandez

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13. ACEs or ARBs for diabetics with overt nephropathy and IHD?

? **Would you use an ACE inhibitor or an ARB as a first-line treatment in a diabetic with overt nephropathy and IHD?**

Submitted by:
Diane Zatelny, MD
Barrie, Ontario

The 2003 Canadian Diabetes Association (CDA) clinical practice guidelines state that the preferred agent is an angiotensin-converting enzyme (ACE) inhibitor in Type 1 diabetes. In Type 2 diabetes, either an ACE inhibitor or an angiotensin receptor blocker (ARB) can be used if the creatinine clearance is > 60 mL per minute, but only use an ARB if the creatinine clearance is ≤ 60 mL per minute.

The Canadian Hypertension Education Program guidelines state that an ACE inhibitor or an ARB are the preferred initial medications for diabetic nephropathy. For patients with diabetes at high risk for cardiovascular disease, an ACE inhibitor is recommended for vascular protection by the CDA guidelines.

Answered by:
Dr. Vincent Woo

14. Cephalosporin use in patients with penicillin allergy

? **Discuss the use of cephalosporins, by history and by skin test, in patients with penicillin allergy.**

Submitted by:
William Moore, MD
London, Ontario

Cephalosporins share the common β -lactam ring with penicillins; however, their clinical cross-reactivity rate is lower than previously thought (< 5%). In most patients with a history of a penicillin reaction, the likelihood of a cephalosporin reaction would depend on the type of reaction. A delayed maculopapular rash is common with penicillins and is likely related to the interplay between the effects of concomitant infections on immune effector cells, along with unique side-chains to that penicillin (most commonly being amoxicillin). In these types of reactions, cross-reactivity is likely very low and cephalosporins may be tried under close surveillance. However, if a reaction is suggestive of an IgE-mediated mechanism, testing should be considered.

A meta-analysis of 11 studies showed cephalosporin reactions in six out of 135 patients (4.4%) with a positive skin test for penicillin, compared with two out of 350 patients (0.6%) with negative skin tests. For patients who require a cephalosporin and have a history of an IgE-mediated reaction to penicillin, the options are desensitization with the selected cephalosporin or a graded challenge, which confers a small but real risk of anaphylaxis.

Answered by:
Dr. Tom Gerstner

15. Bone loss screening for patients on long-term antiepileptic drugs?

Should we routinely screen young patients for bone loss on long-term anti-epileptic drugs?

Submitted by:
Ruth Adler, MD
Kitchener, Ontario



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There is increasing evidence that exposure to antiepileptic drugs (AEDs) is a risk factor for the development of osteoporosis. Among other effects, these medications interfere with vitamin D metabolism through the up-regulation of the CYP24 gene, a mitochondrial enzyme responsible for inactivating vitamin D metabolites.

One study¹ showed that long-term AEDs in younger male patients (mean age of 45) causes significant bone loss at the hip, independent of:

- vitamin D deficiency,
- smoking, or
- alcohol intake.

However, there is a paucity of data on which to base absolute recommendations on screening.

The 2002 Osteoporosis Society of Canada guidelines classify these patients as having a “minor” risk factor for osteoporosis. Therefore, to follow the guidelines strictly, only the subgroup of patients on AEDs and with a major risk factor (e.g., fragility fracture or positive family history) or an additional minor risk factor (e.g., low dietary calcium or smoking) should be screened.

However, in light of the more recent data, we feel it may be reasonable to obtain a baseline bone-mass density in these patients, since one would expect that there may be progressive bone loss over time and that these patients will require ongoing monitoring. In addition, younger patients should all be counselled on the importance of exercise and adequate calcium intake (1500 mg q.d.) and vitamin D (800 IU q.d.).

References

1. Andress DL, Ozuna J, Tirschwell D, et al: Antiepileptic drug-induced bone loss in young male patients who have seizures. *Arch Neurol* 2002; 59(5):781-6.


Answered by:
Dr. Elizabeth Hazel
Dr. Michael Starr

16. Borderline personality disorder treatments

? What treatments are available for borderline personality disorder?

Submitted by:
Bill Taylor, MD
 Medicine Hat, Alberta

Different treatments are available for borderline personality disorder, which means that no one treatment has proven universally effective. During a crisis situation, when a borderline individual experiences a severe narcissistic injury following a perceived rejection, the potential for suicide, self-harm or a brief psychotic breakdown becomes high. In this situation, a brief, crisis hospitalization for a few days, combined with the administration of an atypical anti-psychotic medication (*i.e.*, olanzapine) in small dose (*i.e.*, 2.5 mg to 5 mg q.d.), would resolve the crisis.

In between crises, psychological treatment—either individually or, preferably, in group therapy—would be helpful. Cognitive-behavioral therapy has been tried, with some success. Recently, dialectical-behavioral therapy, based on a biosocial theory that borderline symptoms primarily reflect dysfunction of the emotion-regulation system, has shown superiority in both reducing core symptoms and in increasing social adjustment of borderline patients. Sometimes, combining psychological therapy with a small dose of a selective serotonin reuptake inhibitor, such as 20 mg of fluoxetine q.d., or 10 mg of escitalopram oxalate q.d., may prove beneficial in reducing the disorder's affective lability and thus, enables the patient to better tolerate and benefit from the psychotherapy sessions. 

Answered by:
Dr. Hany Bissada