



Answers to your questions
from our medical experts

1. Long-term effects of PPI usage



What are the long-term effects of continuous PPI usage?

Submitted by: [Shirley S. Gee, MD](#), Edmonton, Alberta

The concerns of long-term proton pump inhibitor (PPI) use mainly revolve around the risks of neoplasia. Long-term PPI use causes hypergastrinemia in humans, but without consequence. However, hypergastrinemia in rats has caused gastric carcinoids. Rats should be aware of long term use of PPIs!

Extended PPI use has been shown to change *Helicobacter pylori* gastritis from antral predominant to corpus predominant. There is no evidence that PPI usage leads to

cancer through atrophic gastritis or any other means.

There is a potential for bacterial overgrowth in the anacidic stomach.

Long-term PPI use has been associated with an increased risk of pneumonia, though, to-date, a direct causal relationship has not been established.

Answered by: [Dr. Robert Bailey](#); and [Dr. Ali Cadifi](#)

2. Dealing with shift work and sleep



What is the best medication for shift work insomnia (requiring daily use)?

Submitted by: [R. Lewans, MD](#), Victoria, British Columbia

The treatments for shift work are complex and vary with the type of work schedule (*i.e.*, fixed work on an evening or night shift, vs. progressively cycling shifts from day to evening to night shifts). Various strategies have been tried and found to be helpful, including:

- napping before going into work for an evening shift, or
- taking a scheduled nap during a regular nighttime workshift.

Using bright lights during nighttime shift work and avoiding light during the day have been proposed for nighttime shift workers.

Following this same principle, nighttime shift workers are encouraged to wear sun glasses while driving home in the morning to avoid exposure to intense daylight before going to bed.

In terms of medication, melatonin has been found to be less successful than timed bright light exposure in aiding adjustment to shift work.

Answered by: [Dr. Hany Bissada](#)

3. Diagnosing intestinal cystitis



How to diagnose intestinal cystitis?

Submitted by: J. Gray, MD, Vancouver, British Columbia

Interstitial cystitis (IC) is a clinical syndrome characterized by daytime and nighttime urinary frequency, urgency and pelvic pain of unknown etiology. The pathophysiology and diagnostic criteria of IC are unclear; no specific clinical or urinary markers, radiographic, laboratory, or serologic findings or biopsy patterns exist that are pathognomonic for IC.

IC is a diagnosis of exclusion and is most often made when the long-standing symptoms of urinary frequency, urgency and pelvic pain exist in the absence of a readily identifiable etiology, such as a urinary tract infection. Urinalysis and urine culture are mandatory. A voiding diary is helpful in establishing baseline voiding frequency. Cystoscopy could help in making the diagnosis, but its use is somewhat controversial due to a lack of specific or pathognomonic findings (except perhaps the very rare finding of a Hunner ulcer). Urodynamic evaluation is optional and finding detrusor overactivity or pelvic floor dysfunction may suggest an alternative diagnosis.

Because no pathognomonic criteria exists for the diagnosis of IC, the modified National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK) criteria for the inclusion of patients in IC studies can be used. These include specific cystoscopic findings under anesthesia and pain associated with either the bladder, urinary urgency and the absence of any of the following criteria:

- Cystometric bladder capacity > 350 mL in a conscious subject with either gas or liquid filling

- Intense urge to void when patient's bladder has been filled with 100 mL of gas or 150 mL of water during cystometry at a fill rate of 30 mL/minute to 100 mL/minute
- Demonstration of phasic involuntary bladder contractions on cystometry findings at a fill rate of 30 mL/minute to 100 mL/minute. (Note that although this is an exclusion criterion as per the NIDDK, detrusor instability may be present in as many as 14% of patients with a clinical diagnosis of IC)
- Duration of symptoms for less than nine months
- Nocturia
- Symptoms relieved by antimicrobials, urinary antiseptics, anticholinergics, or antispasmodics
- Frequency of micturition of less than eight times per day
- Diagnosis of bacterial prostatitis or cystitis within a three-month period
- Presence of ureteral or bladder calculi
- Active genital herpes
- Uterine, cervical, vaginal, or urethral cancer
- Urethral diverticulum
- Cyclophosphamide or other chemical cystitis
- Tuberculous cystitis
- Radiation cystitis
- Benign or malignant bladder tumours
- Vaginitis
- Patient < 18-years-of-age

Answered by: [Dr. Hugues Widmer](#)

4. ACE inhibitors and anaphylaxis



Why do ACE inhibitors blunt the response to adrenaline in anaphylaxis?

Submitted by: [Keith M. Laycock, MD](#), Mill Bay, British Columbia

β -blockers are known to potentially increase the severity of anaphylaxis, or perhaps more accurately, make treatment more difficult, due to the blocking of β -receptors in the heart and vasculature where adrenaline acts to reverse hypotension. Such patients can experience:

- refractory hypotension,
- bradycardia and
- relapsing manifestations.

It is possible that patients using angiotensin-converting enzyme (ACE) inhibitors may also experience more severe anaphylaxis, although this is less well-established. The mechanism may be similar to that which

occurs in patients who experience cough or angioedema while on these medications (incidence 0.1% to 0.2%). By inhibiting angiotensin converting enzymes, ACE inhibitors promote the accumulation of bradykinin and other vasoactive peptides that may, in part, account for the reactions associated with ACE inhibitors. Angiotensin receptor antagonists have not been associated with a significant incidence of cough or angioedema and are usually tolerated by those who have cough and angioedema from ACE inhibitors.

Answered by: [Dr. Tom Gerstner](#)



5. Cause of oro-pharyngeal cancer

What is the cause of oro-pharyngeal cancer? Does HPV play a part?

Submitted by: [A. John B. Nazareth, MD](#), Toronto, Ontario

The strongest risk factors for oro-pharyngeal/upper aerodigestive tract cancers (also known as head and neck cancers) remain to be smoking and alcohol. In terms of viral etiologies, the HPV, especially subtype 16, can be detected in a portion of head and neck squamous cell carcinomas, including cancers of the oral cavity and is believed to play

an etiological role. The effects of these risk factors (*i.e.*, smoking and HPV) may be additive.

Resource

1. Herrero R, Castellsague X, Pawlita M, et al: Human papilloma virus and oral cancer: The International Agency for Research on Cancer multicenter study. *J Natl Cancer Inst* 2003; 95(23):1772-83.

Answered by: [Dr. Sharlene Gill](#)



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6. Eosinophilic pneumonia



I have a patient who was diagnosed with eosinophilic pneumonia. What is the etiology? How do you treat the disease? What is its usual course?

Submitted by: **Victor Voon, MD**, Coquitlam, British Columbia

A wide variety of disorders are associated with acute eosinophilic pneumonia, often with peripheral eosinophilia. These disorders include:

- parasitic (e.g., toxocara, filaria, strongyloides, *Ascaris*) and fungal infections (e.g., *Aspergillus*),
- viral (e.g., HIV, coxsackie),
- toxin and medication reactions (e.g., various antibiotics, L-tryptophan, phenytoin, inhalation of heroine or crack cocaine) and
- idiopathic acute eosinophilic pneumonia.

Many other conditions can be associated with the recovery of high numbers or percentages (> 5% of differential cell count) of eosinophils in bronchoalveolar lavage fluid (BALF) during bronchoscopy, including:

- idiopathic pulmonary fibrosis,
- sarcoidosis,
- systemic lupus erythematosus,
- Churg-Strauss syndrome,
- Graft-vs.-host-disease and
- allergic bronchopulmonary aspergillosis.

Idiopathic acute eosinophilic pneumonia is typically an acute febrile illness of short duration associated with hypoxia, bilateral airspace opacities on chest radiograph and evidence of eosinophilia on BALF, or lung biopsy without an identifiable etiology.

This condition is usually very responsive to treatment with systemic corticosteroids (e.g., in the absence of acute respiratory failure, 0.5 mg/kg to 0.75 mg/kg q.d. of oral prednisone for four to six weeks, then tapering by 5 mg weekly until discontinued). Higher doses of corticosteroids are used in acute respiratory failure.

Chronic eosinophilic pneumonia (CEP) is a separate disorder characterized by dyspnea, cough and constitutional symptoms, often seen in a patient with a preceding history of asthma. Chest radiograph shows peripheral, bilateral airspace opacities. Both peripheral blood and BALF eosinophilia are present. As with acute eosinophilic pneumonia, CEP is responsive to treatment with systemic corticosteroids, although the duration of therapy required is longer and relapses are common after the drug is discontinued. Some patients require long-term therapy with low-dose prednisone.

Prognosis is usually good with treatment, although it is rare that individuals will develop acute or chronic respiratory failure.

Resource

1. Goetzl EJ, Luce JM: Eosinophilic Lung Diseases. In Murray JF, Nadel JA (eds.): *Textbook of Respiratory Medicine*, Third Edition. W.B. Saunders Company, Philadelphia, 2000, pp. 1757-73.

Answered by: **Dr. Paul Hernandez**

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7. Which antidepressant for a diabetic?



What is an ideal antidepressant for a depressed patient with diabetes?

Submitted by: J. Srinivasan, MD, Toronto, Ontario

There are no specific guidelines as to an ideal antidepressant for the treatment of a depressed patient with diabetes. However, it would be prudent to avoid antidepressants that tend to cause weight gain, which is usually undesirable in diabetes. Among the selective serotonin reuptake inhibitors, paroxetine is known to facilitate weight gain.

Answered by: Dr. Hany Bissada

8.

The health risk of expired medications



Regarding expired medications, other than a decreased efficacy, is there a significant health risk?

Submitted by: Paul Keeley, MD, St. Catharines, Ontario

Medication expiration dates are not unlike “best before” dates on food. Expiration dates reflect close to 100% efficacy until that date, with proper exposure to:

- light,
- moisture and
- temperature.

The regulations indicate a maximum five-year stability period in the US and Canada. However, some products that are properly stored and maintained may retain potency for > 10-years.

Most drugs disintegrate over time, such as acetylsalicylic acid that develops a vinegar-like odour as it degrades. Radioisotopes may only last hours-to-days.

Tetracycline-type antibiotics, for example, can cause serious toxicity if taken beyond the expiration date. Expired tetracyclines may cause Fanconi syndrome. As well, extra antibiotics lying around may increase the risk

of microbial resistance due to non-compliance. Depending on the coating, tablets and capsules may be hygroscopic (absorb moisture) but are generally more stable than liquids.

So, the answer is that it depends. One must consider the risk-benefit assessment.

Resources

1. Expired prescription medication. www.associatedcontent.com/article/5236/expired_drugs_are_they_safe.html. Accessed March 17, 2007.
2. Montoliu J, Carrera M, Darnell A, et al: Lactic acidosis and Fanconi's syndrome due to degraded tetracycline. *Br Med J (Clin Res Ed)* 1981; 283(6306):1576-7.
3. Pechère JC: Patients' interviews and misuse of antibiotics. *Clin Infect Dis* 2001; 33(Suppl):S170-3.
4. JT Carstensen, CT Rhodes (eds): *Drug Stability: Principles and Practices*, Third Edition. In: *Drugs and the Pharmaceutical Sciences*. Volume 107. Marcel Dekker Inc, New York, 2000.

Answered by: Professor Joel Lamoure

9. OP screening in men



What are the recommendations for OP screening in men?

Submitted by: [Jeffrey King, MD](#), Kitchener, Ontario

While more common in women, osteoporosis (OP) is still a significant problem in men. In fact, for unknown reasons, the mortality associated with hip fractures is higher in men than in women.

The Osteoporosis Society of Canada's position is that bone mineral density (BMD) measurement is recommended in all men and post-menopausal women > 50-years-of-age with one major or two minor risk factors, as well as for all women and men > 65-years-of-age. Note that the BMD measurement guidelines were designed to compare results with young women and so it is unclear how to apply current BMD guidelines to men.

If low bone density is found in men, it is appropriate to consider secondary causes (which are much more common in men than in women). Therefore, a measurement of the following may be necessary depending on the case:

- serum testosterone,
- calcium,
- alkaline phosphatase,
- protein electrophoresis,
- vitamin D and
- renal and hepatic function.

Answered by: [Dr. Michael Starr](#)

Fasting plasma glucose can have its ups and downs



monday a.m.



tuesday a.m.



wednesday a.m.

People with diabetes have often found it difficult to keep their glucose readings consistent – even with excellent diabetes management habits. To make matters worse, many patients with inconsistent fasting plasma glucose levels can still have near-normal A1C results. This frustrating reality creates uncertainty for doctors and patients alike.¹

REFERENCE: 1. Russell-Jones D. Insulin detemir: improving the predictability of glycaemic control. *International Journal of Obesity* 2004;28(Suppl 2):S29-S34.

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10. What causes cracks in a tongue?



What causes cracks to appear in a patient's tongue? Any treatment advice?

Submitted by: **Morag E. Goldie, MD**, Calgary, Alberta

A cracked or fissured tongue, also known as lingua plicata, is a condition frequently seen in the general population. It is characterized by a short or long deep central groove on the dorsal tongue with multiple irregular side grooves. The grooves can vary in depth and the deeper portions of the grooves are often depapillated which can contribute to bacterial overgrowth and inflammation.

The prevalence of a fissured tongue has been reported to be 5% to 11% in dental studies. A fissured tongue is a normal finding with ageing and is also the most common developmental defect of the tongue. It has also been associated with:

- Sjögren syndrome,
- Down syndrome,
- acromegaly,
- psoriasis,
- geographic tongue and
- Melkersson-Rosenthal syndrome.

Patients with a fissured tongue are usually asymptomatic and the condition is often noted as an incidental finding. Unless there is something on history to suggest an associated syndrome, no further investigation is necessary, particularly in older patients. Patients should be reassured of the benign nature of the condition.

Treatment consists of brushing the tongue after meals with a soft-bristled toothbrush to prevent a buildup of food debris and bacteria in the fissures. Not doing so can lead to halitosis and even pain if food gets lodged in the fissures. If pain is a problem when eating, a topical anaesthetic (e.g., lidocaine viscous) can be applied.

Resource

1. Rogers RS, Bruce AJ: The tongue in clinical diagnosis. *J Eur Acad Dermatol Venereol* 2004; 18(3):254-9.

Answered by:

Dr. Robert Bailey; and Dr. Matt Butler

11. Which parameter is most important in hypothyroidism?



In the treatment of hypothyroidism, which parameter is most important in adjusting thyroid supplement dosage (T4, liothyronine or TSH)?

Submitted by: **Sandra Lee, MD**, Winnipeg, Manitoba

The best and most reliable parameter to follow in most patients is the thyroid stimulating hormone (TSH). After initiation or dose change of levothyroxine (T4), the TSH may take a number of weeks to get to a new steady state level. Therefore, the TSH can be

checked six to eight weeks after initiation or a dose adjustment.

Answered by: **Dr. Vincent Woo**

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12. When to refer to a urologist



In the past they said to refer to a urologist only when PSA was > 4 ng/ml. Has the number now changed to 2.5 ng/ml?

Submitted by: F. Perrault, MD, Ste. Anne de Bellevue, Quebec

Prostate specific antigen (PSA) is a molecule (kallikrein-like serine protease) produced almost exclusively by the epithelial cells of the prostate. It is organ-specific, but not cancer-specific and can be elevated in other benign conditions of the prostate, as in prostatitis or benign prostate hyperplasia, for example.

Although PSA testing is not perfect, it, combined with a digital examination, remains the best screening tool available for prostate cancer. There is no universally accepted lower cut-off value, although > 4 ng/ml has been used in many studies. Lower thresholds have been proposed, especially for younger men because it is known that the risk of harbouring prostate cancer is 22% to 30% and 41% for PSA values of 2.5 ng/ml to 4 ng/ml and 4 ng/ml to 10 ng/ml, respectively. Lowering the threshold raises the issue of the possibility of detecting insignificant cancers whose natural history are not life-threatening and also the possibility of doing a higher number of biopsies that will, in turn, be negative.

In order to maintain the pros of PSA testing while lowering the cons, modifications of PSA are being studied, such as:

- free PSA,
- PSA density,
- PSA velocity,
- age specific values, etc.

Although these modifications are promising, a consensus has yet to be reached regarding their application in clinical practice. As a general rule, men < 60-years-of-age should be referred to a urologist if their PSA values are > 2.5 ng/ml. For men > 60-years-of-age, a threshold of 4 ng/ml can be maintained.

In all cases, life expectancy should exceed 10 years if treatment is to be offered.

Answered by:
Dr. Hugues Widmer; and Dr. Pierre I. Karakiewicz

There is no universally accepted lower cut-off value, although > 4 ng/ml has been used in many studies.

13. Stem cell transplant and multiple myeloma



How does a stem cell transplant help multiple myeloma?

Submitted by: [Michael Manjos, MD](#), Toronto, Ontario

Stem cell transplantation, most commonly autologous peripheral stem cell transplantation, has been associated with an increased rate of remission and prolonged survival when compared to standard chemotherapy alone. However, this approach is not associated with curative eradication of multiple myeloma. Criteria for selecting patients appropriate for high-dose chemotherapy with stem cell rescue include:

- young age (typically < 75-years) and
- advanced stage (Durie-Salmon stage II or III).

Eligibility for autologous transplantation should be considered as part of the upfront assessment for patients with newly-diagnosed multiple myeloma.

Answered by: [Dr. Sharlene Gill](#)

14. Antihistamine use following a yellow-jacket sting



Which antihistamine is probably the most helpful in those with systemic allergic symptoms following a yellow-jacket sting?

Submitted by: [Graham White, MD](#), Parksville, British Columbia

As a rule, antihistamines play little role in reducing the severity of systemic venom reactions.

Injectable epinephrine is critical in this setting to reduce the mortality and morbidity of severe venom allergic reactions.

The role of an antihistamine would be to improve cutaneous symptoms of pruritis and urticaria. Diphenhydramine, given intravenously, would be the standard choice, given its rapid onset of action.

For mild urticarial eruptions, cetirizine has a similar onset as well as the advantage of being non-sedating and longer-acting.

Answered by: [Dr. Tom Gerstner](#)

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15. Who requires a DEXA scan?



Should a 60-year-old man who weighs 60 kg and has a family history of OP have a DEXA scan?

Submitted by: **S. Sullivan, MD**, Victoria, British Columbia

Osteoporosis (OP) is less well studied in men than in women; however, the 2002 Canadian Osteoporosis Practice Guidelines have made recommendations pertaining to men. These guidelines recommend that all men > 65-years-of-age be screened with a dual energy x-ray absorptiometry (DEXA). Also, all those < 65 years-of-age, who present with one of the major risk factors listed below should be screened with a DEXA scan (CMAJ 2002):

- vertebral compression fracture,
- fragility fracture after age 40,
- family history of osteoporotic fracture (especially maternal hip fracture),
- systemic glucocorticoid therapy greater than three months duration,

- malabsorption syndrome,
- primary hyperparathyroidism,
- propensity to fall,
- osteopenia apparent on x-ray film and
- hypogonadism.

Using these guidelines, the answer to the above question of whether a 60 kg, 60-year-old man with a family history of OP should be screened is “no,” unless the family history is that of an osteoporotic fracture or there exists an endocrine or other major risk factor to warrant screening him.

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

16. ACE inhibitors, Type 1 diabetes and children



What is the youngest age at which ACE inhibitors are indicated for Type 1 diabetes? Have they been studied in children?

Submitted by: **Kyra Roeck, MD**, North Vancouver, British Columbia

Diabetic nephropathy is rare in prepubertal children, regardless of the duration of diabetes or glucose control. Other causes of proteinuria must be sought prior to making this diagnosis. As well, intermittent albuminuria is higher during early puberty.

Abnormal screening results require confirmation and follow-up to demonstrate persistent microalbuminuria. Treatment is indicated only for those adolescents with persistent microalbuminuria.

There are very few studies of angiotensin-converting enzyme (ACE) inhibitors in adolescence and those that exist are relatively short-term, but they do show reduced microalbuminuria. Therefore, treatment of adolescents with persistent microalbuminuria is based on the effectiveness in adults with Type 1 diabetes.

Answered by: **Dr. Vincent Woo**

17. Determining the dose for testosterone replacement



What is the best way to determine the appropriate dose for testosterone replacement? Lab test? Patient symptoms?

Submitted by: Terry Holman, MD, Bracebridge, Ontario

Both laboratory tests and a patient's symptoms should be monitored to determine the appropriate dose for testosterone replacement therapy. The laboratory test used depends on the testosterone assay available locally. The desired time of measurement also depends on the type of testosterone replacement, such as:

- injections,
- scrotal or skin patches and
- gels.


Both laboratory tests and a patient's symptoms should be monitored to determine the appropriate dose for testosterone replacement therapy.

Upon taking the above into consideration, the level of testosterone should be titrated into the normal range. In the case of intramuscular injections, the level should be assessed half way until the next dose is scheduled. Luteinizing hormone levels can also be checked in patients with primary hypogonadism.

Patients should be assessed for:

- virilization,
- libido,
- muscle strength and endurance and
- general sense of well being.

Bone density measurements may also be measured if indicated, but it can obviously take some time (one year) for a change to occur.

Side-effects also need to be assessed and include local symptoms of the injection site or skin or scrotal areas where the testosterone treatment is given. Exacerbation of acne and gynecomastia have been reported. Psychological effects, such as aggressive behaviour may also occur. Erythrocytosis may occur and a hemoglobin and hematocrit should be performed regularly. Prostate size will likely increase with therapy. A prostate exam before, at three months time and then annually, should be performed and a prostate specific antigen level checked regularly. 

Answered by: Dr. Vincent Woo



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