



*Answers to your questions  
from our medical experts*

## 1. HPV and anal carcinoma

### ? Is HPV a precursor to anal carcinoma?

Submitted by: **Earl Hutchinson, MD**, New Westminster, British Columbia

Yes. Human papillomavirus (HPV) infection is strongly associated with squamous cell carcinoma of the anal canal, particularly subtype HPV 16. This risk may be further facilitated by concomitant HIV infection and post-transplant immunosuppression.

Of note, women with a history of cervical cancer, which is also strongly associated with HPV infection, may be at an increased risk for anal cancer.

Answered by: **Dr. Sharlene Gill**

## 2. How to treat resistant depression

### ? How to manage resistant depression (can we use between two and three selective serotonin reuptake inhibitors [SSRIs])?

Submitted by: **Rukevwe Ugwumba, MD**, Regina, Saskatchewan

Once a major depression is diagnosed, then an antidepressant is prescribed, the dose of which will be gradually increased until it reaches the recommended therapeutic dose. If no improvement is obtained after an appropriate interval of time (usually four weeks), then the dose will be increased to the maximum allowed dose, provided it is reasonably well tolerated by the patient.

If there is still no improvement, then we are likely managing a resistant depression. In this case, the following treatment options are to be considered:

- If the patient reports no improvement at all on the highest possible dose of the antidepressant, that particular antidepressant should be stopped. The physician can then switch the patient to a different antidepressant, preferably one that will target a different neurotransmitter (e.g., switching from a SSRI to a serotonin-noradrenaline reuptake inhibitor [SNRI])
- If the patient reports a modest improvement on the highest recommended dose of a SSRI, then the treating physician may choose to augment that SSRI with another antidepressant that targets a different neurotransmitter (e.g., a dopamine reuptake inhibitor, such as bupropion or a SNRI, such as venlafaxine)
- If augmentation with a second antidepressant has not been effective, or is not well tolerated by the patient, then the augmentation can be done by adding a mood stabilizer, such as lithium or olanzapine. The latter is also considered a mood stabilizer in addition to being an atypical neuroleptic
- If all the above fail, then electroconvulsive therapy may be considered for a severe depression that is resistant to pharmacological treatment

Answered by: **Dr. Hany Bissada**

### 3. Polyneuropathy and osteoporosis



**A 41-year-old female suffers from chronic inflammatory polyneuropathy. She was recently put on 150 mg of methylprednisolone twice a week for eight weeks and 150 mg once a week for eight weeks. Should I put her on bisphosphonates to prevent osteoporosis?**

Submitted by: [Diane Giroux, MD](#), Montreal, Quebec

In patients receiving corticosteroids, fracture risk has been associated with doses as low as 2.5 mg of prednisone q.d. The 2002 Canadian Osteoporosis Guidelines recommend initiation of bone-sparing therapy with a bisphosphonate in patients receiving > 7.5 mg of prednisone q.d. for more than three months. Patients receiving long-term doses of prednisone > 2.5 mg q.d. were also thought to be at increased risk of fracture and required further assessment (at least a bone mineral density [BMD] scan). The 2000 American College of Rheumatology guidelines differ slightly in that initiation of a bone-sparing agent is recommended at a dose > 5 mg q.d. for more than three months.

If you were to convert the total weekly methylprednisolone dose to a daily prednisone dose, the patient would be receiving the equivalent of 50 mg q.d. for the first eight weeks and then 25 mg q.d. for the next eight weeks. These doses of prednisone would require treatment with a bisphosphonate. However, the issue of bone protection with weekly methylprednisolone administration is not as clear cut.

There are few published reports of the impact of pulse intravenous (IV) methylprednisolone on bone mass. The short exposure time to corticosteroids using pulses of IV

methylprednisolone is thought to be less harmful for the bone and theoretically should not lead to as profound bone loss. However, in an observational study, Haugeberg, *et al* showed a statistically significant reduction in BMD in patients receiving pulse methylprednisolone for rheumatic diseases (*e.g.*, systemic lupus erythematosus and vasculitis) (Ann Rheum Disease 2004). These patients all received only six pulses of high dose methylprednisolone (10 mg/kg) and were all on a baseline low dose of prednisone (mean 5 mg) concurrently. It is unclear from this study whether there was a confounding effect of the constant low-dose prednisone on BMD.

With regards to weekly pulses of smaller (< 5 mg/kg) doses of methylprednisolone, there is no data to support the addition of a bisphosphonate in the absence of any risk factors for osteoporosis. However, this patient should be screened for risk factors and have a baseline BMD. Calcium and vitamin D supplementation should also be initiated and there should be a low threshold to start treatment, should any risk factors be present.

Answered by: [Dr. Sabrina Fallavollita](#); and [Dr. Michael Starr](#)

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## 4. Ginseng use to prevent common colds?



### What is the evidence supporting ginseng use to prevent upper respiratory tract infections?

Submitted by: [Ira Smith, MD](#), Toronto, Ontario

A recent Health Canada survey conducted by Ipsos-Reid of > 2000 adult Canadians revealed that 71% had used natural health products in the past.<sup>1</sup> Many herbal remedies (including preparations of the plant echinacea and roots of ginseng) are promoted to have beneficial immunomodulatory effects, but few have been rigorously studied in the prevention and treatment of the common cold. A Cochrane review of echinacea found inconsistent results of efficacy in both

treatment and prevention of the common cold.<sup>2</sup> In contrast, three recent randomized, controlled trials have shown significant clinical benefits in terms of preventing acute upper respiratory tract illness in adults taking a proprietary extract of roots of North American ginseng when compared with placebo.<sup>3-5</sup>

For references and resources, please contact [diagnosis@sta.ca](mailto:diagnosis@sta.ca).

Answered by: [Dr. Paul Hernandez](#)

## 5. Which insulin to use?



### What is the best insulin to start a patient on (e.g., a Type 1 diabetic)?

Submitted by: [Frank J. Foley, MD](#), Toronto, Ontario

Insulin therapy for individuals with both Type 1 and Type 2 diabetes must be individualized. One must evaluate a host of factors when deciding which insulin to choose and how often insulin is to be administered. Some of these factors include:

- target glycemetic control,
- age,
- cultural concerns,
- occupation,
- other medical conditions,
- cost,
- life expectancy,
- risk of hypoglycemia and
- oral anti-hyperglycemic agents, etc.

There are also a number of insulins now available, from rapid-acting insulins to long-acting insulins. As well, there are a number of pre-mixed insulins that have a combination of rapid or fast-acting insulin combined with an intermediate-acting insulin.

Insulin is used to improve glycemetic control while trying to avoid hypoglycemia. Patient education is very important and the use of diabetes educators and pharmacists is essential.

Answered by: [Dr. Vincent Woo](#)

## 6. Which meds for irritable bladder?



**Is there a medication that can be used as needed for irritable bladder/urgency of psychologic etiology (*i.e.*, in particular/specific stressful situations)?**

Submitted by: **Mark Saffer, MD**, Thornhill, Ontario

Irritable bladder is due to uninhibited contraction of the detrusor muscle and spasticity of the external sphincter and pelvic floor muscles, causing incoordination of the function of micturition. The condition could be due to organic causes (*e.g.*, bladder infection, interstitial cystitis or other neurological causes). However, it is very common for this condition to be due to psychological causes, including severe anxiety and exposure to situations perceived by the patient to be stressful or threatening.

Unfortunately, there is no drug of choice to treat irritable bladder of psychological etiology. Ideally, psychological treatment like cognitive-behavioural therapy (CBT) should be offered to address the patient's perception of threat in specific stressful situations. CBT could also be combined with bladder retraining which consists of developing a schedule of times when the patient should try to urinate, while trying to consciously delay urination between these scheduled times.

If psychological treatment and bladder retraining are not helpful, then a medication trial on some anticholinergic agents would be justified. Tricyclic antidepressants, such

as imipramine or doxepine, at small doses (10 mg to 25 mg q.d.), could be prescribed for their anticholinergic effect. Alternatively, tolterodine could be prescribed at a dose between 1 mg to 2 mg b.i.d. p.o.

As mentioned earlier, these are not drugs of choice for irritable bladder of psychological origin. Patients with closed angle glaucoma, urinary retention and hepatic impairment should not receive these drugs. The most common side-effects of anticholinergic medications are:

- dry mouth,
- constipation,
- abnormal vision (accommodation abnormalities),
- dizziness,
- palpitations and
- urinary retention in predisposed patients.

Answered by:  
**Dr. Hany Bissada**

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## 7.

### Can a vasectomy impair athletic performance?



**Has vasectomy been shown to cause any impairment to athletic performance over time?**

Submitted by: **John T. Jenkins, MD**, Lunenburg, Nova Scotia

Vasectomy is a very effective contraception method. Moreover, it is a simple procedure that can be done under local anesthesia. Most patients can resume normal activities after a few days. Complications related to the surgery include hematomas (1%), infections (one in 500 cases), re-permeabilisation of the vasa deferentia and chronic discomfort. This latter complication occurs in about 4% of the patients who have undergone a vasectomy. It is most often intermittent and most often can be relieved with mild analgesia and

very rarely requires vasectomy reversal. Although this discomfort can be a concern to patients, there is no evidence that vasectomy should affect athletic performance, nor is it associated with diminished sexual performance or reduction in orgasm sensation. Furthermore, no link has been shown between vasectomy and genitourinary cancers, nor systemic diseases.

Answered by:  
**Dr. Hugues Widmer**

## 8.

### Can diabetic peripheral neuropathy be reversed?



**Is diabetic peripheral neuropathy reversible once glycemic control is established?**

Submitted by: **Donald Greve, MD**, Rosthern, Saskatchewan

For the prevention of diabetic peripheral neuropathy, optimal glycemic control is likely the best way that this complication can be avoided. Many studies have shown this to be true, but the best study to specifically evaluate this was the Diabetes Control and Complications Trial which correlated the glycosylated hemoglobin with the development of diabetic peripheral neuropathy in individuals with Type 1 diabetes.

Once peripheral neuropathy has occurred, the course of this complication can be quite

variable. However, improving glycemic control has improved nerve conduction studies and patient symptoms. There are many medications available for the symptoms of painful peripheral neuropathy, though they do not alter the underlying pathophysiology.

Other reversible causes of neuropathy should be sought out (e.g., hypothyroidism, B12 deficiency and nerve compression).

Answered by:  
**Dr. Vincent Woo**

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## 9. Psyllium allergies



### How common are allergies to psyllium, as it is being used in everything from laxatives to cereals?

Submitted by: **John E. Dawson, MD**, Ottawa, Ontario

Recent interest in psyllium has arisen primarily due to its use in high-fiber breakfast cereals and from claims that these high fiber cereals containing psyllium are effective in reducing cholesterol. Allergic reactions from handling psyllium have been reported since 1970. Health professionals and workers in laxative-manufacturing plants are at greatest risk. Sensitized people are at risk of life-threatening anaphylactic reactions. From the multiple case reports published, most of these patients were atopic and most often worked in the healthcare setting (in particular, nurses). James, *et al* published a case series of 20 women, mainly nurses, who reported reactions to psyllium. Symptoms developed shortly after small amounts of the cereal were ingested and most commonly included moderate-to-severe wheezing, throat and chest tightness and urticaria. Specific IgE antibodies to various psyllium protein fractions were documented in all the subjects. It was concluded that individuals sensitized by occupational exposure to psyllium dust are at high risk for allergic

reactions to ingested psyllium-containing products.

Malo, *et al* reported on the prevalence of sensitivity to psyllium for chronic care hospitals. A questionnaire and skin prick tests with psyllium and various inhalants were administered to 193 of 248 (78%) of the workers who agreed to participate. The authors found that the prevalence of IgE sensitization to psyllium was between 5% (skin testing) and 12% (increased specific IgE levels). The incidence in the general population is unknown, but would be higher in the atopic population and in those with a history of significant exposure to psyllium.

#### Resources

1. James JM, Cooke SK, Barnett A, et al: Anaphylactic reactions to a psyllium-containing cereal. *J Allergy Clin Immunol* 1991; 88 (3 Pt 1):402-8.
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3. Malo JL, Cartier A, L'Archeveque J: Prevalence of occupational asthma and immunologic sensitization to psyllium among health personnel in chronic care hospitals. *Am Rev Respir Dis* 1990; 142(6 Pt 1):1359-66.

Answered by:  
**Dr. Tom Gerstner**

*Allergic reactions from handling psyllium have been reported since 1970. Health professionals and workers in laxative-manufacturing plants are at greatest risk. Sensitized people are at risk of life-threatening anaphylactic reactions.*

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## 10. BMD testing for women on medroxyprogesterone?



### Is BMD testing required for women on long-term medroxyprogesterone?

Submitted by: [Safaa Loka, MD](#), Mississauga, Ontario

Medroxyprogesterone is a contraceptive injection which suppresses estrogen levels. Studies have shown that women on medroxyprogesterone have lower bone density and long-term users < 21-years-of-age had the lowest bone density, especially if they started at a young age. However, it appears that bone density recovers when it is stopped and there are no studies that answer the question of whether its early use leads to fragility fractures in later life.

The World Health Organization has suggested that medroxyprogesterone be used with caution in women < 18 years and > 45-years-of-age and that alternative means of contraception be considered if possible.

Regarding bone mineral density (BMD) measurement, it is not practical or useful to

recommend scanning all women on medroxyprogesterone. Yet, in some situations BMD testing may be appropriate since the results may influence management decisions. For example, women who have other risk factors for osteoporosis may benefit from BMD testing so that those with a bone density that is already low can consider alternative methods of contraception. It may also be appropriate to test women using medroxyprogesterone who are approaching menopause since this is a time when risk of osteoporosis may be increasing.

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

## 11. Men, estrogen and breast cancer



### I have a man on estrogen for gender dysphoria. Is he at risk for breast cancer?

Submitted by: [James Simon, MD](#), Okotoks, Alberta

While the use of unopposed estrogen therapy has been associated with an increased risk of breast cancer amongst post-menopausal women, the risk in men on such therapy is unknown. However, one would assume that the risk may be theoretically higher and may be additive to other known

risk factors for male breast cancer, including breast cancer 2, early onset (BRCA2) gene, first-degree family history, testicular dysfunction and prior radiation.

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

## 12. Diagnosing hyperaldosteronism



### What investigations would you recommend to diagnose hyperaldosteronism?

Submitted by: **Enrique Guerra, MD**, Leamington, Ontario

Primary hyperaldosteronism refers to a renin-independent increase in the secretion of aldosterone as opposed to secondary hyperaldosteronism, where aldosterone secretion follows a renin rise (renovascular hypertension). Approximately 99% of cases of primary hyperaldosteronism are due to either an aldosterone-producing adenoma (approximately 40% of cases) or idiopathic hyperaldosteronism (approximately 60% of cases, almost all of which are due to bilateral adrenal hyperplasia).

Primary aldosteronism should be suspected in patients with hypertension and unexplained hypokalemia, but also in patients with severe or resistant hypertension and in patients with adrenal incidentaloma. It is characterized by hypokalemia (although up to 50% of patients can be normokalemic), suppressed plasma renin activity and a high serum and urinary aldosterone level after sodium repletion.

The main screening test consists of measuring the aldosterone/renin ratio. If this ratio

is increased, confirmation of the diagnosis is achieved by measuring the 24-hour urinary aldosterone after three days of adequate sodium intake, or by measuring the aldosterone levels after intravenously loading with 2 L of normal saline. The potassium deficit has to be corrected and interfering medication discontinued before performing these tests. It is important to differentiate between an adenoma and bilateral hyperplasia as surgery is suggested for the adenoma while hyperplasia is treated medically. A CT or MRI scan of the adrenals are considered reasonable imaging tests. If a unilateral macroadenoma > 1 cm is identified and the contralateral adrenal is completely normal, the most likely diagnosis is unilateral aldosterone-producing adenoma requiring surgery. An abnormality in both glands, an adrenal mass < 1 cm or lack of radiological changes may reflect bilateral disease. In such cases, selective catheterization of the adrenal veins with venous sampling can help define the diagnosis. The adrenal venous sampling is an invasive technique requiring skillfull intervention (especially for the catheterization of the right adrenal vein) and should be performed in experienced centers. Some centers prefer performing venous sampling in all patients to avoid unnecessary surgery.

*Approximately 99% of cases of primary hyperaldosteronism are due to either an aldosterone-producing adenoma or idiopathic hyperaldosteronism.*

Answered by:  
**Dr. Hugues Widmer, and Dr. Hortensia Mircescu**



## 13. Food-induced rhinitis



**I've been told that gustatory (food-induced) rhinitis and vasomotor rhinitis are closely related. Will ipratropium bromide nasal spray help both conditions?**

Submitted by: [Paul Stephan, MD](#), Scarborough, Ontario

Isolated food-induced rhinitis is almost never an allergic phenomenon. Hot and spicy foods most commonly trigger nasal symptoms in those patients with vasomotor rhinitis. The predominating symptom is copious, clear rhinorrhea, usually provoked by noxious stimuli (other examples include strong smells/fumes from various fragrances, various chemicals, extreme cold air) which, in part via cholinergic pathways, increase

serous mucous production in the nasal mucosa. These patients often respond well to topical nasal anticholinergic therapy (*i.e.*, nasal ipratropium bromide), often requiring four times daily dosing initially and is best used just prior to exposure to the known aggravating triggers (*e.g.*, before meals).

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

## 14. Measuring serum calcium



**By measuring serum calcium, can I tell if a patient has enough calcium for their bones to be maintained?**

Submitted by: [Paul Stephan, MD](#), Scarborough, Ontario

Serum calcium, even ionized serum calcium, would not be reflective of a patient's calcium intake because of the interaction of parathyroid hormone (PTH), 1,25-hydroxycholecalciferol and calcitonin with target tissues such as the kidney, gut and bone, to decrease or increase blood calcium levels. When calcium intake is low, increased bone turnover and resorption of calcium occurs in order to maintain good homeostasis.

The best method of measuring adequate calcium intake in patients for good bone health would be by measuring markers of bone turnover, such as serum alkaline phosphatase, osteocalcin and deoxypyridinoline. Although their role in osteoporosis is not yet well established, abnormalities in these

values may reflect inadequate calcium intake in the setting of normal PTH and vitamin D levels. However, these markers are not routinely used for this purpose.

The daily recommended dose of calcium is 1 g q.d. Patients who have difficulty taking oral supplements should be encouraged to increase their dietary intake of calcium. Diets high in phosphate, which binds calcium and prevents its absorption and increases bone turnover should also be avoided. Patients should be counselled to take their calcium supplements after meals to optimize absorption (particularly calcium carbonate).

Answered by:  
[Dr. Sabrina Fallavollita](#); and [Dr. Michael Starr](#)

# 15. Role of diet in diverticulosis



## What is the role of diet in patients with diverticulosis?

Submitted by: **Denis Petrunia, MD**, Victoria, British Columbia

Uncomplicated diverticulosis, (*i.e.*, incidentally found diverticular disease in an asymptomatic patient), has a 10% to 25% risk of progressing to diverticulitis. A classic study by Burkitt<sup>1</sup> (while in Uganda) found that the incidence of diverticular disease was substantially lower, but that the mean fibre intake and mean stool bulk was much higher than Europeans. In fact there have been descriptions by Painter, *et al*<sup>2</sup> of increasing diverticulosis prevalence as Western diets shifted to more refined ingredients since the industrial revolution.

Only recently has the role of insoluble fibre in reducing complications of diverticulosis been studied. The data from randomized controlled trials<sup>3,4</sup> looking at the administration of a high fibre diet to patients with diverticulosis is sparse, but seems to support its use. The risk of progression to diverticulitis also increases with the amount of red meat ingested and decreases with physical activity as described by the large Health Professionals Follow-up Study.<sup>5</sup>

Although conceptually intuitive, the actual risk of whole fibre pieces, such as nuts and seeds, in triggering diverticulitis is unknown. Diets avoiding these types of foods have yet to be investigated.

Thus, for this extremely common disease process, we have only to offer a high fibre diet and exercise as a means of reducing the risks of complications.<sup>6</sup>

### References

1. Burkitt D: Diverticular disease of the colon epidemiological evidence relating it to fibre-depleted diets. *Trans Med Soc Lond* 1973; 89:81-4.
2. Painter NS, Burkitt DP: Diverticular disease of the colon: A deficiency disease of Western civilization. *BMJ* 1971; 2:450-4.
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4. Ornstein MH, Littlewood ER, Baird IM, et al: Are fiber supplements really necessary in diverticular disease of the colon? *Br Med J (Clin Res Ed)* 1981; 282(6276):1629-30.
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6. Stollman PJ, Raskin J: Diagnosis and management of diverticular disease of the colon in adults. *Ad Hoc Practice Parameters Committee of the American College of Gastroenterology. Am J Gastroenterol* 1999; 94(11):3110-21.

Answered by:  
**Dr. Robert Bailey; and Dr. Harvey Hawes**

*Although conceptually intuitive, the actual risk of whole fibre pieces, such as nuts and seeds in triggering diverticulitis is unknown. Diets avoiding these types of foods have yet to be investigated.*

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## 16. Celiac disease in children



**How common is celiac disease in children? What symptoms should we be looking for? Are blood tests a good first-line screening approach?**

Submitted by: **Andrea Coholic, MD**, Timmins, Ontario

According to the American Gastroenterology Association, prevalence may be as high as approximately one in 150 in specific populations. Individuals most at risk originate from Ireland, the United Kingdom, Italy or Sweden and tend to have other autoimmune diseases or genetic conditions such as Down syndrome or Turner syndrome.

In children, classic symptoms include watery diarrhea and failure to thrive. However, it is now well established that the symptoms can be quite subtle. Anemia, weight loss, dermatitis herpetiformis and osteopenia may occur in the absence of these classic symptoms. In addition, celiac sprue should be considered in all individuals with Type 1 diabetes, not only as a second autoimmune phenomenon, but also because dietary gluten restrictions will aid in glucose/insulin regulation.

First-line testing currently involves antibody testing. Studies done by Dieterich, *et al* have shown that antitransglutaminase antibody testing has a sensitivity and specificity of 90% to 98% and 95% to 97% respectively. Other blood tests include antiendomysial and anti gliadin antibodies. As all of these antibodies are IgA antibodies, it is prudent to ensure that the individual is not subtly IgA-deficient by

*The prevalence of celiac disease in children may be as high as approximately one in 150 in specific populations.*

ordering quantitative immunoglobulin levels (thereby preventing false negative results). However, the gold standard for diagnosis still remains small bowel biopsy showing villous atrophy which improves following a three to four month period of dietary gluten restriction.



#### Reference

1. Dieterich W, Laag E, Schopper H, et al: Autoantibodies to tissue transglutaminase as predictors of celiac disease. *Gastroenterology* 1998; 115(6):1317-21.

Answered by: **Dr. Robert Bailey; and Dr. Marilyn Zeman**