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## Diagnosing Chronic Cough in a Nonsmoking Adult

1.

### What is the diagnostic approach to chronic cough in a nonsmoking adult?

Question submitted by:

**Dr. Miguel Lipka**

**Victoria, British Columbia**

The answer to this question is long and complex, but, in brief, a careful history and examination might reveal a cause. For example, a history of treatment with ACE inhibitors for hypertension would point to a likely cause, especially if the chest radiograph is normal. With a normal chest radiograph, a good next step would be to examine lung function with spirometry. If the clinical assessment, chest radiograph, and spirometry are normal, we are generally left with a range of conditions that have laryngeal irritation in common. Laryngeal irritation may occur without an obvious precipitating cause, but it is often associated with gastroesophageal reflux or chronic upper respiratory tract disease. Several studies have emphasized that many of these cough patients may have gastroesophageal reflux without having obvious symptoms.

In many centres, there is a chronic cough clinic that concentrates on patients with normal findings and chronic cough. The assessment and management are complex and usually include measures to decrease laryngeal irritation. In some instances, a speech pathologist/therapist may be of assistance.

This may be a very debilitating disorder that often has a negative impact on the patient's social life and ability to work. Chronic cough may cause additional problems, such as stress incontinence and even rib fractures. This condition certainly deserves very careful assessment.

Answered by:

**Dr. Robert Cowie and Ms. Diane Conley, RRT, CRE, Respiratory Education Consultant, Chronic Cough Clinic, University of Calgary**



## ACE Inhibitors for the Prevention of Cardiomyopathy?

2.

**Is it useful to use ACE inhibitors to try and prevent cardiomyopathy from certain chemotherapy protocols?**

Question submitted by:  
**Dr. A Swan**  
*Fredericton, New Brunswick*

Currently, this is an area of unmet need; however, ACE inhibitors are not currently used for cardio protection in this setting given the very limited evidence available of their effectiveness. A small study of 473 cancer patients treated with various high-dose chemotherapy regimens<sup>1</sup> evaluated the use of enalapril in a subset of 114 patients with an elevated serum troponin I. This subset of patients was randomized 1:1 to one year of enalapril versus no treatment, and patients in the intervention arm had a preserved left ventricular ejection fraction (LVEF) compared with declines in LVEF in the nonintervention arm.<sup>1</sup> The ongoing Prevention of Cardiac Dysfunction During Adjuvant Breast Cancer Therapy trial, a randomized, placebo-controlled, 2 x 2 factorial design Phase II trial evaluating candesartan (angiotensin receptor blocker) and metoprolol ( $\beta$ -blocker) in patients with early stage breast cancer receiving anthracycline-based chemotherapy (epirubicin) with or without trastuzumab, may shed further light in this area.<sup>2</sup>

### References

1. Cardinale D, Colombo A, Sandri MT, *et al*: Prevention of High-dose Chemotherapy-induced Cardiotoxicity in High-risk Patients by Angiotensin-converting Enzyme Inhibition. *Circulation* 2006; 114(23):2474–2481.
2. Prevention of Cardiac Dysfunction During Adjuvant Breast Cancer Therapy (PRADA) <http://www.clinicaltrials.gov/ct2/show/NCT01434134>. Accessed: March 12, 2013.

Answered by:  
**Dr. Roger Y. Tsang**

## Following the $\beta$ -hCG of a Patient with a Suspected Abortion

3.

**After a suspected abortion, do we have to follow  $\beta$ -hCG?**

Question submitted by:  
**Dr. Galley Anik**  
*Roberval, Québec*

For a suspected abortion, a transvaginal/pelvic US is important to confirm that products of conception have not been retained and that no ectopic pregnancy nor trophoblastic molar pregnancy is present. Once a spontaneous abortion has been confirmed and there is no evidence of an ectopic or molar pregnancy, the  $\beta$ -hCG should return to normal within one to eight weeks depending on the gestational age (GA) of the aborted embryo or fetus. The  $\beta$ -hCG is highest at 8 to 10 weeks GA, so a return to normal will be longer from this time. Usually, it is not necessary to repeat the  $\beta$ -hCG unless the woman presents with symptoms of bleeding, pain, or other pelvic discomfort. In this case, the  $\beta$ -hCG can be repeated with an US. There are rare conditions where the  $\beta$ -hCG will remain slightly elevated for months or years, such as preceding an indolent trophoblastic state, but this is rare. If the  $\beta$ -hCG level rises, this must be investigated with imaging, such as US.

Answered by:  
**Dr. Cathy Popadiuk**

## Tricuspid Valve Insufficiency

**4.**

### **What are the various causes of tricuspid valve insufficiency, and when should we intervene?**

Question submitted by:

**Dr. Diane Giroux**  
**Montréal, Québec**

Despite the fact that tricuspid regurgitation (TR) is one of the most commonly encountered valvular problems in clinical practice and is readily diagnosed with echocardiography, it has not received as much attention as either the aortic or mitral valves and has been dubbed the “forgotten valve.” Causes of TR include primary valve pathology, including rheumatic injury, myxomatous degeneration, endocarditis (often related to illicit IV drug use), congenital heart disease (Ebstein’s anomaly), and the carcinoid syndrome, as well as functional TR secondary to pulmonary hypertension, right ventricular enlargement with tricuspid valve annular dilation, or valvular coaptation interference from pacemaker/implantable cardioverter defibrillator wires. **Functional TR is the most frequent etiology of tricuspid valve pathology seen in Western countries, and it is most often related to primary mitral valve disease. Although significant TR may be clinically silent for a prolonged period, severe TR can lead to progressive right ventricle dilatation and dysfunction, liver congestion, and pedal edema.** Tricuspid valve repair is beneficial for severe TR in patients with mitral valve (MV) disease requiring MV surgery, and either replacement or annuloplasty repair is indicated for severe, primary TR when symptomatic.

Answered by:

**Dr. Theodore K. Fenske**



## Loss of Taste and Smell Following Upper Respiratory Infection

5.

**A 57-year-old male had an upper respiratory infection, followed by a loss of taste and smell. What could be the cause, and what advice should I offer?**

Question submitted by:

**Anonymous**

While most people who experience a loss of smell may only be aware of the sensory loss, many will also notice a loss or change in taste, since taste is highly connected to the sense of smell. Anosmia could be congenital (e.g., Kallmann syndrome: 1:50,000 female and 1:10,000 male). The main causes of acquired anosmia are:

1. Nasal and/or sinus disease (nasal polyposis, sinusitis)
2. Previous upper respiratory infection
3. Idiopathic
4. Head trauma

A viral upper respiratory infection can cause extensive scarring and replacement of the olfactory epithelium, but studies suggest that stem cells remain, allowing for potential regeneration of the olfactory epithelium. Recovery of smell/taste in these cases can take weeks to months, and, in some instances, it may never occur.

Endocrine disturbances may also be addressed by administration of the deficient hormone, as with hypothyroidism. Diabetes mellitus may slow neural degeneration of the olfactory system. Tobacco smoking impairs the ability to identify odors. Occupational exposure to chemicals may also lessen the sense of smell. Lead poisoning, drugs (amphetamines, estrogen, naphazoline, phenothiazines, prolonged use of nasal decongestants, etc.), radiation therapy, nasal or sinus surgery, tracheotomy, and nasal or brain tumours may be the cause. Finally, like vision and hearing, the senses of smell and taste become less accurate with aging.

Some unproven remedies have been attempted; the best known of these is zinc sulfate. Its use is controversial, and it has not been proven effective in the absence of a specific zinc deficit. Idiopathic cases of olfactory loss are not amenable to specific treatment. Other remedies include pharmacologic doses of vitamins, steroid (systemic or local spray), and tricyclic antidepressants (for their effect on cerebrospinal fluid and catecholamines).

Answered by:

**Dr. Ted Tewfik**

## Outgrowing Allergies

**6.**

### Why is it that children are more likely to outgrow their allergies than adults?

Question submitted by:

**Dr. Anette Lam**

**Vancouver, British Columbia**

The question of why children are more likely to outgrow their allergies than adults is a difficult one to answer, because no one knows for certain why this is the case. Perhaps the best theory relates to immune plasticity in children. Like the brain in young children, which is thought to have more plasticity or adaptability than the relatively fixed adult brain, the immune system in children seems to have a degree of plasticity or adaptability that allows it to be modified over time. It has been suggested that immune maturity does not occur until age five or older; thus, there is a greater ability to lose items from immune memory before that age. The finding that many children “outgrow” their milk and egg allergies by about the age of five would certainly fit with this theory. However, not all childhood allergies are outgrown and some, such as those to nuts, peanuts, and shellfish, are less likely to be lost from immune memory and may persist into adulthood. While the theory of immune plasticity seems to explain why some children outgrow their allergies, no one knows for sure if this is the real reason for this observed phenomenon.

Resource

1. The author gathered some of the information presented above in a conversation with Michael Rieder, MD, PhD, FRCPC, FAAP, FRCP(Glasgow), on July 4, 2013.

Answered by:

**Dr. Krista Helleman**



## Treating IBS Patients with Metronidazole

7.

**Could you comment on trying to treat IBS patients with metronidazole? They have small intestine bowel overgrowth.**

Question submitted by:

**Dr. Mitch Rubin**

**Vancouver, British Columbia**

Evidence implicating gastrointestinal bacteria and the human microbiome in the pathophysiology of a variety of functional and inflammatory gastrointestinal diseases has progressively evolved. Within this body of literature, small intestinal bacterial overgrowth (SIBO) has been hypothesized as a contributing etiology of IBS. Up to 84% of subjects diagnosed with IBS have SIBO (as defined by lactulose breath testing), with data from meta-analysis of case-controlled studies demonstrating abnormal breath testing as being more common in IBS subjects than controls.<sup>1-3</sup> The strongest association between hydrogen excreting enteric flora and symptoms has been found in patients with IBS-diarrhea, whereas methane-associated SIBO has a high positive predictive value for IBS-constipation.

In the context of a bacterial hypothesis in IBS, a growing body of literature suggests that antibiotics may have an important therapeutic role in treatment. Several broad-spectrum antibiotics have been used successfully to treat bacterial overgrowth (including metronidazole), although their therapeutic use has been limited by systemic absorbability and the side effect and resistance profiles.<sup>4</sup> A recent meta-analysis of five studies of the poorly absorbable antibiotic rifaximin demonstrated greater efficacy in global IBS symptom improvement versus placebo (odds ratio = 1.57; 95% confidence intervals = 1.22, 2.01; therapeutic gain = 9.8%; number needed to treat = 10.2).<sup>5</sup> Adverse effects were similar among patients receiving rifaximin or placebo in all studies.<sup>5</sup> The modest therapeutic benefit from rifaximin treatment was similar to that from other currently available therapies for IBS.<sup>5</sup> Overall, this area of therapeutic treatment represents a promising domain in IBS management, and further data is anxiously awaited to facilitate integration into current treatment paradigms.

### References

1. Pimentel M, Chow EJ, Lin HC: Eradication of Small Intestinal Bacterial Overgrowth Reduces Symptoms of Irritable Bowel Syndrome. *Am J Gastroenterol* 2000; 95(12):3503–3506.
2. Pimentel M, Chow EJ, Lin HC: Normalization of Lactulose Breath Testing Correlates with Symptom Improvement in Irritable Bowel Syndrome: A Double-blind, Randomized, Placebo-controlled Study. *Am J Gastroenterol* 2003; 98(2):412–419.
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4. Van Citters GW, Lin HC: Management of Small Intestinal Bacterial Overgrowth. *Curr Gastroenterol Rep* 2005; 7(4):317–320.
5. Menees SB, Maneerattannaporn M, Kim HM, *et al*: The Efficacy and Safety of Rifaximin for the Irritable Bowel Syndrome: A Systematic Review and Meta-analysis. *Am J Gastroenterol* 2012; 107(1): 28–35.

Answered by:

**Dr. Theodore Xenodemetropoulos**

8.

## A Patient with Factor V Leiden Mutation

**I have a young patient on warfarin for factor V Leiden deficiency. He would like to get a tattoo. Is this safe?**

Question submitted by:  
**Dr. Steven E Bowen**  
*Calgary, Alberta*

The factor V Leiden mutation is a common mutation of the normal clotting factor, factor V, that occurs in approximately 5% of the Caucasian population. This mutation confers resistance to inactivation by the body's normal anticoagulation system by activated protein C. Hence, individuals with this mutation have an increased risk of thrombosis. The relative risk of thrombosis compared to the general population is increased by three- to five-fold in a heterozygous person and up to 80-fold in a homozygous person. However, other factors can increase the risk of thrombosis, such as age, smoking, obesity, and use of estrogen-based oral contraception.

In general, patients with the factor V Leiden mutation do not require anticoagulation unless they develop a thrombosis. In general, precautions should also be taken to prevent a thrombosis in high-risk situations, such as during surgery, hospitalization, and pregnancy. If this patient has a reason for anticoagulation, such as a remote thrombosis, then his warfarin can be held five days prior to any procedure (such as a tattoo) and resumed the following day. If there has been a recent thrombotic event, then it would be advisable to postpone the procedure for at least four to six weeks. If there are any concerns, a referral to a thrombosis specialist is warranted.

Answered by:

**Dr. Cyrus Hsia and**  
**Dr. Kang Howson-Jan**

## Hepatitis B and Hepatocellular Carcinoma

**9.**

**Should we screen a chronic hepatitis B carrier by US for hepatocellular carcinoma (hepatoma) every year after a certain age (e.g. > 50)?**

Question submitted by:

***Anonymous***

Hepatitis B is an important cause of hepatocellular carcinoma (HCC). Antiviral therapy should be considered for cases of hepatitis B (HBV), since response to treatment is associated with a lower risk for HCC. However, treatment rarely eradicates the infection, and screening for HCC is often indicated. The major risk factor is cirrhosis, and all cirrhotic patients should be screened. Additional recommendations for screening from the American Association of Liver Diseases include Asian men over the age of 40, Asian women over the age of 50, patients with HBV and cirrhosis, African and North American blacks, and patients with a family history of HCC. It is unclear what to do with Caucasians who generally have a lower risk for HCC. Some suggest limiting screening to those with persistently high viral loads or alanine aminotransferase, using the same age restrictions used for Asians. The recommended screening method is ultrasonography every six months. In many Canadian jurisdictions, this frequency of testing is difficult to provide, and the frequency must be adjusted accordingly. It should be noted that the recommended interval is a function of the typical rate of growth of tumours and not the risk of HCC, so it is not entirely logical to use longer intervals for patients at lower risk. It should also be noted that the use of  $\alpha$ -fetoprotein measurements does not appear to provide any additional benefit.

Answered by:

**Dr. Michael Libman**





## A Patient with Type II Diabetes and Dyslipidemia

10.

**A 46-year-old man who has type II diabetes and hypercholesterolemia has a coronary CT angiography. It reveals a noncalcified plaque in the left anterior descending artery. He is put on a statin. What will the statin do for the plaque?**

Question submitted by:

**Dr. Louis Marin**  
**Saint-Jean-sur-Richelieu,**  
**Québec**

This is an interesting question. This man with type II diabetes and dyslipidemia has a very high risk for coronary artery disease. Even without angiographic results, a statin would be indicated. In this case, his CT coronary angiography revealed a noncalcified plaque (otherwise known as a soft plaque). Acute cardiac ischemic events most frequently arise from either rupture or erosion of the surface of a soft plaque, which leads to localized platelet aggregation and acute thrombosis.

The statins, particularly atorvastatin and rosuvastatin, have been shown in numerous studies to reduce coronary plaque volume. In several noninvasive studies, plaque calcification has actually been increased with statin therapy. In addition, statins have been shown to have a direct effect on the arterial endothelium, helping to restore the normal balance between vasoconstrictor and vasodilation effects of the endothelium. In effect, the statins will delay the progression of arterial disease, actually reducing plaque volume and stabilizing the plaque and the surface endothelium, which reduces the chance of rupture or erosion, thus, reducing the likelihood of acute coronary events.

Answered by:

**Dr. Wayne Warnica**



## Biopsy of a Thyroid Nodule

11.

### When is a biopsy necessary for a thyroid nodule?

Question submitted by:  
**Dr. Sameera Benjamin**  
Woodbridge, Ontario

It does not matter if the nodule was found by observation/clinical exam or incidentally on a radiographic study. Generally, only nodules greater than 1 cm should be evaluated, as they are much more likely to be clinically significant if they are malignant, making this a cost-benefit decision. Increased malignancy risk occurs if there is a history of radiation to the head or neck, the history of a first-degree relative having thyroid cancer, or the presence of worrisome lymphadenopathy. Hoarseness or observed rapid growth is worrisome. A fine-needle aspiration (FNA) is suggested for most nodules with a solid component over 1 cm, assuming the serum thyroid stimulating hormone is not suppressed, which makes it possible for a functioning nodule (which is almost always benign) to be present. Hence, a thyroid scan should be done. Ultrasonographic features that may be mostly associated with malignancy include nodule hypoechogenicity, increased nodular vascularity, irregular margins or absent halo, or the presence of microcalcifications. Benign features on US include a pure cystic nodule or a spongiform appearance (multiple microcystic components). FNA is not suggested for subcentimeter nodules, unless there are worrisome clinical or ultrasonographic features.

#### Resource

1. Revised American Thyroid Association Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid* 2009; 19(11):1167–1214.

Answered by:

**Dr. Bernard Corenblum**

## Eyelid Dermatitis

12.

### What are common causes of eyelid dermatitis?

Question submitted by:  
**Dr. Steve Choi**  
Oakville, Ontario

Eyelid dermatitis can be the result of a variety of causes, such as atopic dermatitis, seborrheic dermatitis, and irritant dermatitis (dry air, harsh soaps, topical retinoid creams). The eyelid skin is thin and subject to sensitization to allergens, such as shampoos (formaldehyde and fragrance), eye medications, hair dyes, makeup, and airborne allergens like pollens. Many triggers for eyelid allergy result from allergens being rubbed on the eyelids by the hands. These allergens include nickel, nail polish, and rubber. Therefore, a detailed history, examination, and appropriate patch testing is needed to establish a clear analysis of recurrent eyelid dermatitis.

Answered by:

**Dr. Scott Murray**

*cme*