Answers to your questions from our medical experts

1. Effect of antihistamines on anaphylaxis

Will an antihistamine, taken immediately after a wasp sting, block angioedema?

Submitted by:
William Fair, MD
Vernon, British Columbia

Antihistamines block histamine receptors and as such, they have no effect on established allergic inflammation, including airway or tissue edema. Even if given early, they usually do not modify the course of anaphylaxis, nor are they effective at preventing significant angioedema. Their main usefulness lies in modifying a subsequent urticarial eruption and reducing pruritus. Unfortunately, when some patients are given the choice between a potential life-saving maneuver (self-administered adrenaline) and ingesting an oral medication that will not reverse anaphylaxis, they make the unfortunate choice of an antihistamine, delaying more effective treatment. In fact, for this very reason, we are now suggesting that patients with serious food and venom allergies need not carry an antihistamine. This will increase the likelihood that they will use the more appropriate medication, their self-injectable epinephrine.

Answered by:
Dr. Tom Gerstner

2. Fecal DNA testing for colorectal cancer?

What is the status of fecal DNA testing as a screening test for colorectal cancer?

Submitted by:
Craig Render, MD
Kelowna, British Columbia

There is a great deal of interest in developing stool-based molecular screening tests. Fecal DNA testing looks for genetic abnormalities associated with carcinogenesis in shed DNA from colorectal neoplasms. While in commercial development, fecal DNA testing is limited by its high cost. It is cumbersome and has a less than optimal sensitivity for cancer of approximately 50%. Therefore, at present, it is not recommended in any screening guidelines for colorectal cancer.

Answered by:
Dr. Sharlene Gill

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3. Iron absorption

A 45-year-old menopausal woman with inflammatory arthritis has iron-deficiency anemia (*i.e.*, low iron, low ferritin). Her GI workup is negative for blood loss. She takes iron supplements, 300 mg t.i.d. (with orange juice) without any improvement. She takes PPIs for reflux. Why is she not absorbing the iron?

Submitted by:
Monique Moreau, MD
Alliston, Ontario

This patient may have persistent iron-deficiency anemia, despite iron supplementation, for three reasons:

1. An ongoing obscure GI bleed that was missed on her standard GI workup
2. A GI disorder (*i.e.*, celiac disease) that is preventing her from absorbing the iron supplements
3. The proton pump inhibitors (PPIs) are inducing hypochlorhydria which impairs the absorption of orally-administered nonheme iron in iron-deficient individuals

In post-menopausal women, the GI tract is the commonest site for hemorrhage causing iron-deficiency anemia. Standard workup includes:

- gastroscopy,
- colonoscopy and
- barium studies of the small bowel.

These tests are not without their limitations.

In the past, subtle lesions of the small intestine have been missed. Push enteroscopy and capsule endoscopy are currently considered to be the most effective diagnostic procedures to find obscure causes of iron deficiency from a small bowel cause. The diagnostic yield of push enteroscopy, in the investigation of obscure GI bleeding, ranges from 38% to 75%. A prospective study showed that capsule endoscopy has a sensitivity, specificity, as well as positive and negative predictive values of 95%, 75%, 95% and 86%, respectively.

Malabsorptive disorders, such as celiac disease, can also cause iron-deficiency anemia. A recent study of 331 patients with iron-deficiency anemia of unclear origin, showed that 47.5% of them actually had celiac disease that was diagnosed on the basis of histological findings and antibodies. For your particular patient, failure to diagnose and treat the underlying disease will result in persistent iron-deficiency anemia, even with adequate iron supplementation.

Orange juice has the potential to enhance serum iron levels, as ascorbic acid has the ability to reduce ferric-to-ferrous iron improving absorption, whereas PPIs may potentially impair iron absorption by producing a hypochlorhydric state. To date, clinical studies have failed to associate PPIs with iron deficiency, even with prolonged use. In summary, this patient should undergo appropriate diagnostic studies to rule out ongoing blood loss and celiac disease.

For resources, please contact **diagnosis@sta.ca**.

Answered by:
Dr. Robert Bailey

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4. Lipid-lowering agents for diabetics?

Should all diabetics take lipid-lowering agents?

Submitted by:
Stephen MacGregor, MD
Kitchener, Ontario

Clinical practice guidelines from the Canadian Diabetes Association, regarding dyslipidemia in adults with diabetes, were recently published in September 2006. These guidelines were harmonized with the Canadian Cardiovascular Society guidelines that were also published in the same month. Among the recommendations were:

- Most adults with Type 1 diabetes or Type 2 diabetes should be considered at high-risk for vascular disease. The exceptions are younger people with Type 1 diabetes or Type 2 diabetes with a shorter duration of the disease and without complications of diabetes (including established cardiovascular disease [CVD]) and without other CVD risk factors. A computerized risk engine (*e.g.*, UK Prospective Diabetes Study risk engine or Cardiovascular Life Expectancy Model) can be used to better estimate vascular risk
- Patients at high-risk of a vascular event should be treated with a statin to achieve an LDL-cholesterol of (LDL-C) ≤ 2.0 mmol/L. Clinical judgement should be used as to whether additional LDL-C lowering is required for patients with an on-treatment LDL-C of 2.0 mmol/L to 2.5 mmol/L
- The primary target of therapy is the LDL-C; the secondary target is the total cholesterol (TC)/HDL-cholesterol (HDL-C) ratio
- If the TC/HDL-C ratio is ≥ 4.0, consider strategies to achieve a TC/HDL-C ratio < 4.0, such as:
  - improved glycemic control
  - improvement of lifestyle (weight loss, physical activity, smoking cessation) and, if necessary,
  - pharmacologic interventions.

The Canadian Diabetes Association clinical practice guidelines can be accessed on the internet at **www.diabetes.ca.**

Answered by:
Dr. Vincent Woo

5. OTC decongestant medication

Can you comment on the use of OTC decongestant medication in patients with asthma?

Submitted by:
Adam Kayumi, MD
Mississauga, Ontario

Decongestant medications are contained in many over-the-counter (OTC) cold preparations. Asthmatics may turn to these products for temporary relief of symptoms related to an acute upper respiratory tract infection, or inappropriately, to control chronic upper airway symptoms. Chronic upper airway symptoms related to seasonal or perennial allergic rhinitis (AR) are common in asthma. Effective therapies exist for AR, including:

- allergen avoidance,
- intranasal steroids,
- antihistamines,
- leukotriene receptor antagonists and
- immunotherapy.

OTC decongestant medications have a limited role to play in the management of AR. In addition, due to the sympathomimetic properties of OTC decongestants, they should be avoided or used with caution in the elderly or in individuals with comorbidities, such as:

- hypertension,
- diabetes,
- ischemic heart disease,
- stroke,
- angle closure glaucoma, or
- prostatic hypertrophy.

Answered by:
Dr. Paul Hernandez

Due to the sympathomimetic properties of OTC decongestants, they should be avoided or used with caution in the elderly or in individuals with comorbidities.

6. ADHD in adults

When shall I suspect ADHD in an adult? What is the best treatment?

Submitted by:
Ion Soare, MD
Toronto, Ontario

Attention deficit hyperactivity disorder (ADHD) remains a controversial diagnosis and even more so in adults. These patients tend to have repeated conflicts with authorities, leading to frequent job changes; they also have difficulties in intimate relationships and poor frustration tolerance. Frequently, they are misdiagnosed as having a personality disorder or a dysthymic disorder and prescribed selective serotonin reuptake inhibitors (SSRIs) with little or no benefit.

The reality is that ADHD is one of the most common psychiatric diagnosis of adulthood.[1] Current estimates are that 4.1% of adults in the US population have the disorder and the ratio of men-to-women is about 1.5 to 1.0.[1]

Adult manifestations of ADHD include problems with inattention and hyperactivity/impulsivity. Typically, inattentive ADHD adults have problems sustaining attention while in meetings, reading or doing paperwork; yet they are able to hyperfocus on activities that interest them (*e.g.*, spending hours on a video-game). Generally, they are inefficient, with poor time management skills. Hyperactive/impulsive ADHD adults tend to have an inner restlessness, often manifested by rapid changes of jobs and relationships and/or driving too aggressively.

Diagnosing ADHD in adulthood is a clinical process that requires several interviews and data gathering. The onset of symptoms is usually in childhood, before the age of seven years. The clinician must document impairment in at least two aspects of daily life, such as work and family. Psychological tests are helpful, but not diagnostic. Laboratory examinations are important to rule out other medical conditions.

In terms of treatment, medication is essential, provided of course that it is administered in the context of a good therapeutic alliance with the patient to address any negative connotations or prejudices attached to the diagnosis of ADHD.

Central nervous system (CNS) stimulants, namely methylphenidate preparations, or dextroamphetamine preparations, are first-line treatments for adults with ADHD. For patients who cannot tolerate CNS stimulants, or those who have a substance abuse problem, a non-stimulant medication that inhibits noradrenaline reuptake, such as bupropion or atomoxetine, is indicated. SSRIs and venlafaxine are not effective in the treatment of ADHD.

Resource
1. Doyle, Brian B.: *Understanding and Treating Adults with Attention Deficit Disorder*. American Psychiatric Publishing, Inc. 2006.

Answered by:
Dr. Hany Bissada

7. Teriperatide for OP?

What is the role of teriperatide in OP?

Submitted by:
Carol Joyce, MD
St. John's, Newfoundland

Teriperatide is a new anabolic agent used for the treatment of osteoporosis (OP). It is a recombinant human parathyroid hormone which stimulates bone formation. It is administered as a daily subcutaneous injection for 18 months.

It is indicated for the treatment of severe OP in women and for primary or hypogonadal OP in men at high-risk of fracture. Studies show a significant increased bone mineral density (BMD) and decreased vertebral fracture risk. Currently, patients with severe OP (*i.e.*, low BMDs and previous fracture), particularly those not responding adequately to, or who cannot tolerate a bisphosphonate, may be considered as candidates for this treatment.

Answered by:
Dr. Michael Starr

8. Non-rising PSA in hormone therapy

How do you explain non-rising PSA with general metastasis under hormonal therapy?

Submitted by:
Jean-Paul Emond, MD
Lévis, Quebec

Although prostate-specific antigen (PSA) is a very good marker for treatment response and progression in prostate cancer, there are clinical situations in which PSA could be misleading. Most prostate cancer cells will produce PSA and PSA will reflect cancer volume and activity. Thus, an increase in PSA will mean progression and a decrease will mean regression of disease. However, when we deal with high grade, very aggressive cancer (high Gleason grade 8 to grade 10) and/or with neuro-endocrine and small cell prostate cancer, PSA production is often minimal, thus it does not reflect tumor biology. We see this same situation when prostate cancer becomes hormone refractory. These situations will necessitate high suspicion from the clinician. Clinicians rely on patient symptoms, bone scans and radiology to evaluate treatment response and progression, since cancer could be progressing with PSA being low or very low, even with testosterone at castration level.

Answered by:
Dr. Paul Perrotte

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9. Diagnosing primary aldosteronism

What is the best way to diagnose primary aldosteronism?

Submitted by:
Enrique Guerra, MD
Leamington, Ontario

Although this condition is rare, it is important to diagnose. As well, it represents a curable form of hypertension. There are at least four distinct types of primary aldosteronism. The two main types are adrenal aldosterone-producing adenoma (60%) and bilateral micronodular hyperplasia of the adrenals (idiopathic) (40%). Clinically, the presentation includes hypertension and hypokalemia.

The current 2006 Canadian Hypertension Education Program (CHEP) recommendations state that one should screen for hyperaldosteronism in the following situations:

- A hypertensive patient with spontaneous hypokalemia (serum K [potassium] + < 3.5 mmol/L)
- A hypertensive patient with marked diuretic-induced hypokalemia (serum K+ < 3.0 mmol/L)
- Patients with refractory hypertension to three or more drugs
- Hypertensive patients found to have an incidental adrenal adenoma

Screening includes examining plasma aldosterone and renin levels in the arm, in a sitting position, resting for 15 minutes. Antihypertensives are continued prior to testing, except for aldosterone antagonists, angiotensin-receptor blockers, ß-blockers and clonidine.

For patients with suspected hyperaldosteronism (plasma aldosterone/rennin activity ratio > 550 pmol/L/ng/ml/hr), further testing should be done to establish the diagnosis.

Additonal testing details are not included because of space, but include at least one or more of the following:

- Saline loading tests
- Fludrocortisone suppression test
- Plasma aldosterone/plasma renin activity ratio > 1400 with a plasma aldosterone > 440 pmol/L/ng/L
- Captopril suppression test

Localization tests will also be required. Referral to a specialty centre is recommended. Further details of the CHEP recommendations can be found at **www.hypertension.ca.**

Answered by:
Dr. Vincent Woo

10. Aerobic exercise and heart rate

With aerobic exercise, how high can the heart rate get to before it becomes dangerous and for how long?

Submitted by:
Irene D'Souza, MD
Toronto, Ontario

I like to use the Karvonen Formula to determine one's maximum heart rate: 220 - (your age).

To determine one's training heart rate, the formula is: (max heart rate) - (resting heart rate) x (intensity) + (resting heart rate).

The intensity is a percentage of the maximum heart rate. As a general rule, you should exercise at an intensity between 50% to 85% of your heart rate reserve. Your individual level of fitness will ultimately determine where you fall within this range. Use the following as a guide for determining your intensity level:

- Beginner or low fitness level: 50% to 60%
- Average fitness level: 60% to 70%
- High fitness level: 75% to 85%

When you exercise above this level, you do not build aerobic capacity, rather, you stress the heart. Training at > 85% of your maximum heart rate is not sustainable and should only be done under supervised conditions. An exmaple would be a 30-year-old female who has a resting heart rate of 60 bpm and is training at an average fitness level/intensity of 705. Her maximum heart rate would be 220 - (30) = 190. Her training heart rate is 70% of 190 = 133.

Answered by:
Dr. Aly Abdulla

Training at > 85% of your maximum heart rate is not sustainable and should only be done under supervised conditions.

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11. Chronic sinusitis

How does one differentiate between chronic sinusitis of allergic and bacterial causes?

Submitted by:
Irene D'Souza, MD
Toronto, Ontario

Rhinosinusitis lasting > 90 consecutive days is referred to as chronic sinusitis. Chronic sinusitis is characterized by:

- mucosal thickening,
- goblet cell hyperplasia,
- subepithelial fibrosis and
- persistent (often eosinophilic) inflammation.

Activated eosinophils and their by-products are thought to promote the fibrotic changes. Allergic rhinitis is a predisposing factor for rhinosinusitis, implicated in about 20% of all pediatric cases. Nearly 50% of children with refractory chronic rhinosinusitis have positive skin tests to environmental allergens. Current views implicate sensitivity to aeroallergens as an important pathologic mechanism in the development of chronic sinusitis in both children and adults and many studies have shown that the inflammatory substrate in chronic sinusitis is similar to that seen in allergic rhinitis. Risk factors for an allergic cause may be:

- an atopic personal or family history,
- history of naso-ocular symptoms following exposure to various indoor or outdoor allergens, or perhaps
- worsening symptoms during seasonal change.

The most effective way to identify an allergic-provoking factor is via epicutaneous testing (scratch or skin prick testing) to the common aeroallergens.

Answered by:
Dr. Tom Gerstner

Nearly 50% of children with refractory chronic rhinosinusitis have positive skin tests to environmental allergens.

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12. Diagnosing PCO

What is the best way to diagnose PCO? Should we treat PCO with metformin?

Submitted by:
Eleanor Huang, MD
London, Ontario

Polycystic ovary syndrome (PCO) is usually a clinical diagnosis, but diagnostic criteria have been proposed by different groups which should help evaluate clinical trials and other studies of this condition. The National Institute of Health (NIH) in the US proposed consensus criteria in 1990, including:

1. Menstrual irregularity due to oligomenorrhea or anovulation
2. Evidence of hyperandrogenism, either clinical or biochemical
3. Exclusion of other causes of the above two criteria

Therapy must be individualized and depends on the main clinical concern, such as:

- infertility,
- hirsutism,
- obesity,
- endometrial protection and
- glucose intolerence.

Metformin use in this condition is increasing, but at this time, there is no indication for the use of metformin in PCO from Health Canada. There are a number of small or short-term studies, but no large long-term studies. Small studies using metformin for this condition have been associated with improvements in:

- oligomenorrhea,
- hirsutism,
- infertility,
- obesity and
- glucose levels.

Answered by:
Dr. Vincent Woo

Metformin use in this condition is increasing, but at this time, there is no indication for the use of metformin in PCO from Health Canada.

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13. OP and low testosterone in men

Should a middle-aged man with OP and low testosterone be started on hormone replacement therapy or bisphosphonates?

Submitted by:
Adam Kayumi, MD
Mississauga, Ontario

Compared to women, men more frequently have secondary causes for osteoporosis (OP). These can include:

- corticosteroid use,
- alcohol use,
- tobacco use,
- hypogonadism, *etc.*

All men with OP should receive adequate supplementation with calcium (1000 mg, q.d.) and vitamin D (800 u, q.d.). If a secondary cause is found, all efforts should be made to eliminate the offending agent.

In men who have hypogonadism, studies have shown that testosterone replacement increases bone mineral density (BMD). In one study, both markers of bone formation and resorption decreased, suggesting that testosterone has the ability to inhibit bone turnover.

Bisphosphonates are also effective for male OP. One study that compared alendronate to calcium alone found that there was an increased BMD and a reduction in vertebral fractures in men with OP who were treated with the bisphosphonate (about one-third of these men also had slightly low serum testosterone levels). Therefore, it is reasonable to consider bisphosphonates for the treatment of men with OP who do not have hypogonadism, or for hypogonadal men in whom testosterone replacement is contraindicated.

A bone density scan can be repeated one year after therapy in order to monitor changes. Dx

Answered by:
Dr. Michael Starr

In one study, both markers of bone formation and resorption decreased, suggesting that testosterone has the ability to inhibit bone turnover.