Best of 2011

Answers to your questions from our medical experts

1. Cardiac Contraindictions for Adult ADHD Prescriptions

What are the cardiac contraindications to prescribing stimulants for adult ADHD?

Submitted by: Mary Lilley, MD, Toronto, Ontario

Psychostimulants can cause increased blood pressure (particularly in patients with pre-existing hypertension) and cardiac arrhythmias (particularly in individuals with cardiovascular disease). Such effects are not likely in patients without cardiovascular disease or hypertension. Amphetamine is more potent than methylphenidate in producing cardiac or blood pressure effects.

Patients should be screened for cardiovascular risks by history (early cardiac death in the family, family cardiac history, syncope, chest pain upon exertion, *etc.*). If risk factors are present, an ECG and a cardiac consultation should be considered.

In general, psychostimulants are contraindicated in patients with structural cardiac abnormalities or cardiovascular disease, severe angina pectoris, tachyarrhythmias, and severe hypertension.

Resource

1. Drugs for ADHD. In: Virani AS, Bezchlibnyk-Butler KZ, Jeffries JJ (eds.): Clinical Handbook of Psychoactive Drugs. 18th edition. Hogrefe & Huber Publishers, Toronto, 2009, 216–234.

Answered by: Dr. Hany Bissada

2. Negative Anti-tissue Transglutaminase (Anti-tTG)

How long must a person be off wheat (and other gluten grains) to make Anti-tTG negative (in a Celiac patient)?

Submitted by: Bryn Waern, MD, Toronto, Ontario

A patient that is diagnosed with celiac disease often has a positive anti-tTG (tissue transglutaminase) level. It has a high sensitivity and specificity for celiac disease (95% and 94% respectively) and is an excellent test for both the diagnosis and monitoring of celiac disease. Depending on the pretreatment concentration levels, anti-tTG levels will normalize after 3 to 12 months on a strict gluten-free diet.

Caution should be used when using serology tests to monitor response and adherence to therapy. A normal anti-tTG level may not mean normalization of villous atrophy, as mucosa healing is often delayed compared to serology tests. If pretreatment anti-tTG levels are normal, using serology to follow progress is not possible. Serology may not be sensitive enough to measure minor transgressions in the diet, but, if anti-tTG normalizes, it often indicates adherence to the gluten-free diet.

Answered by: Dr. Richmond Sy

3. DVT Risk During Flight

How can we reduce the risk of deep venous thrombosis (DVTs) and ankle edema during flight?

Submitted by: Paul Stephan, MD, Thornhill, Ontario

Philbrick JT, Shumate R, Siadaty MS, *et al,* completed a systematic review on venous thromboembolism (VTE) related to air travel in 2007 and found that these clinical events were rare. They reviewed 24 published reports that analyzed 25 studies on VTE, including 6 case-control studies, 10 cohort studies, and 9 randomized controlled trials. Duration of travel (> 8 hours) and clinical risk had a significant effect on VTE rate. Graduated compression stockings prevented travel-related VTE in four of six studies. Aspirin did not prevent the condition, and low-molecular-weight heparin (LMWH) showed a trend toward efficacy in one study.[1]

These results were echoed in the latest American College of Chest Physicians' (ACCP) guidelines. For travellers who are taking flights over eight hours in duration, general recommendations included avoidance of constrictive clothing around the lower extremities or waist, maintenance of adequate hydration, and frequent calf muscle contraction. For long-distance travellers with additional risk factors for VTE, in addition to these general measures listed above, the ACCP suggested the use of properly fitted, below-knee graduated compression stockings, providing 15 to 30 mmHg of pressure at the ankle or a single prophylactic dose of LMWH injected prior to departure. The ACCP also recommended against the use of aspirin.

These same recommendations may also help with reduction of ankle edema. However, peripheral extremity edema should be investigated further for other underlying causes and managed appropriately.[2]

Resources
1. Philbrick JT, Shumate R, Siadaty MS, *et al*: Air Travel and Venous Thromboembolism: A Systematic Review. J Gen Intern Med 2007; 22(1):107–114.
2. Geerts WH, Berrggvist D, Pineo GH, *et al*: Prevention of Venous Thromboembolism: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest 2008; 133(6 Supl): 381S–453S.

Answered by: Dr. Cyrus Hsia and Dr. Leonard Minuk

4. Heuristic for Treating Skin Conditions

How true is the dermatology saying, "If it's wet, dry it; if it's dry, wet it": as it pertains to treatment of skin conditions?

Submitted by: Katherine Abel, MD, Leduc, Alberta

This old adage is simplistic and exaggerated. With regards to "if it's wet, dry it," it is true that exudative lesions and bullous lesions often need to be compressed to decrease exudation and oozing. However, excessive drying can actually impede wound healing and should be avoided. Compresses are best done with normal saline, as compressing with other astringents may cause toxicity to fibroblasts and again impede, rather than aid in, wound healing.

Currently, healing wounds and ulcers is best managed with the principle of moist wound healing with occlusive dressings using films, foams, hydrocolloids, hydrogels, or alginates.

The old practice of using wet to dry gauze dressing is best avoided. Although this may aid in debridement of ulcers, it can damage new epithelium and angiogenesis and is best abandoned in favour of moist wound healing dressings.

As for "if it's dry, wet it," it is true that moisturizers are very important in treating dry skin and dermatitis, as they help to retain moisture in the epidermis, especially the stratum corneum, and reduce transepidermal water loss by their occlusive effects. However, actual application of moisture to the skin (*i.e.,* wet it) is not helpful and can cause increased dryness due to evaporation of the moisture into the air, unless a moisturizer is used after wetting the skin to retain the moisture. The best time to moisturize is three to five minutes after a shower or bath, while the skin is still damp, which will retain moisture in the stratum corneum. Therefore if it's dry, don't wet it; moisturize it.

Answered by: Dr. Richard Haber

5. Long-term ASA

When should long-term ASA be recommended to patients? There seem to be many grey areas.

Submitted by: C.M. Dewar, MD, O'Leary, Prince Edward Island

Patients with known coronary artery disease (CAD) or ischemic stroke should be on long-term, low-dose ASA (81 mg q.d.) to prevent recurrent vascular events and death related to vascular events.

The debate is whether ASA should be given to patients for primary prevention of stroke and myocardial infarction (MI). ASA decreases the risk of a first MI by 25 to 30%, but it has not been shown to decrease the risk of stroke or cardiovascular death. However, patients who do not have known CAD are at much lower risk for vascular events, and the absolute risk reduction with ASA may be less than the risk of GI bleeding. The excess risk of GI bleed with low dose ASA is up to 0.5% per year. The decision to advise patients to take ASA should depend on their overall risk of vascular events. ASA is recommended for diabetics with one additional risk factor, such as age greater than 40 years, cigarette smoking, hypertension, obesity, albuminuria, hyperlipidemia, or a family history of coronary heart disease, and patients with moderate or high 10-year risk of a coronary event (> 10% risk of MI or cardiac death). ASA should not be given to patients in this risk range when the risk of a GI bleed is higher than the potential benefit in preventing vascular events. Patients at high risk for bleeding from ASA include those older than 60-years-of-age and those with prior history of GI bleed and concurrent use of NSAIDs, steroids, or anticoagulants.

Answered by: Dr. Bibiana Cujec

6. Starting Prediabetics on Metformin

Is it beneficial to start a prediabetic (FBS 6.2 to 7.0) HbA1c < 6.0% on metformin? What dose should be used?

Submitted by: David Apramian, MD, Burk's Falls, Ontario

The loss of 5% of initial body weight through intensive and structured lifestyle modification can reduce the risk of progression from impaired glucose tolerance to type 2 diabetes by almost 60%. Progression from prediabetes to type 2 diabetes can also be reduced by pharmacologic therapy with metformin (~30% reduction), acarbose (~30% reduction), and thiazolidinedione (~60% reduction). A dose of 850 mg b.i.d. was used in the Diabetes Prevention Program.

Answered by: Dr. Vincent Woo

7. Differentiating Between IBS and IBD

Please elaborate on the difference between IBS and IBD, and how to differentiate between the two.

Submitted by: Anna-Viola Dugas, MD, Bathurst, New Brunswick

Irritable Bowel Syndrome (IBS) and Inflammatory Bowel Disease (IBD) are two separate entities, though overlap between the two can occur. Differentiation between these two conditions can be made based on careful history and physical examination, with tailored laboratory and investigative testing.

IBS is part of the spectrum of functional gastrointestinal disorders, characterized primarily by chronic, recurrent abdominal pain and altered bowel habits, in the absence of organic pathological changes. Though the pathophysiology is not entirely clear, proposed mechanisms include abnormalities in gastrointestinal motility, sensation, autonomic function, and serotonin pathways. The Rome III Criteria for diagnosis of IBS requires that patients have recurrent abdominal pain or discomfort at least three days per month, during the past three months, associated with two or more of the following:

- Improvement with defecation
- Onset associated with change in frequency of stool
- Onset associated with change in form (appearance of stool)

This must occur in the absence of warning signs (*e.g.*, anemia, rectal bleeding, weight loss, fever, age > 50, family history of colon cancer or major change in symptoms), which would warrant investigation for organic etiology. Based on evaluation of bowel habits and stool characteristics, patients can be classified into one of three subsets: diarrhea-predominant IBS, constipation-predominant IBS, or mixed subtype.

In contrast, IBD — which includes ulcerative colitis (UC) and Crohn's disease — is characterized by inflammation of the mucosal lining of the gastrointestinal tract. The pathophysiology is thought to be multifocal, with both genetic predisposition and an autoimmune response to a pathologic organism or intraluminal antigen each playing a role. Clinical history typically includes diarrhea (with or without the presence of blood), abdominal pain, tenesmus, weight loss, and, in the case of complicated Crohn's, symptoms of obstruction or perianal disease. Extraintestinal manifestations, such as arthritis, uveitis, and dermatological conditions can be found with both UC and Crohn's. Furthermore, IBD is associated with an increased risk of gastrointestinal malignancy.

Differentiation between the two conditions can be made by the clinical history and laboratory findings, which in IBD may include anemia, increased C-reactive protein, and sometimes leukocytosis. However, the distinguishing factor of IBD is the presence of organic changes: colonoscopy is remarkable for inflammation, erythema, exudates, and ulceration. Microscopic findings of biopsies in IBD feature neutrophilic inflammation, with the presence of crypt abscesses in UC or granulomas in Crohn's disease. In contrast, colonoscopy in IBS will not show any pathologic abnormalities, as this is purely a functional disorder.

References
1. Grundmann O, Yoon SL: Irritable Bowel Syndrome: Epidemiology, Diagnosis and Treatment: An Update for Health-care Practitioners. J Gastroenterol Hepatol 2010; 25(4):691–699.
2. Mayer EA: Clinical Practice: Irritable Bowel Syndrome. N Engl J Med 2008; 358(16):1692–1699.
3. Baumgart DC, Sandborn WJ: Inflammatory Bowel Disease: Clinical Aspects and Established and Evolving Therapies. Lancet 2007; 369:1641–1657.

Answered by: Dr. Robert Bailey and Dr. Marta McCrum

8. Steroids and Bell's Palsy

Is there any evidence-based proof that steroids and antivirals are helpful in Bell's palsy?

Submitted by: **Peter Noble, MD,** Oshawa, Ontario

Inflammation of the facial nerve is considered to be the cause of the symptoms of Bell's palsy, and corticosteroids are helpful in improving these symptoms by reducing the inflammation. There is significant improvement in outcome when prednisone is initiated within 72 hours of the onset of symptoms. Use of antiviral agents is controversial, as some of the previous trials have shown limited benefit, but recent randomized controlled trials showed no benefit.

Suggested Readings

1. Salinas RA, Alvarez G, Daly F, *et al*: Corticosteroids for Bell's Palsy (Idiopathic Facial Paralysis). Chochrane Database Syst Rev 2010; (3): n.p.
2. Adour KK, Ruboyianes JM, Von Doersten PG, *et al*: Bell's Palsy Treatment with Acyclovir And Prednisone Compared with Prednisone Alone: A Double Blind, Randomized, Controlled Trial. Ann Otol Rhinol Laryngol 1996; 105(5):371–378.

Answered by: **Dr. Abdul Qayyum Rana**

9. Disadvantages of Drug-eluting Stents

What are the disadvantages of drug eluting stents?

Submitted by: Keng Sim, MD, Acton, Ontario

Drug-eluting stents are coated with a polymer that contains an antiproliferative drug, such as sirolimus or paclitaxel. These drugs decrease the likelihood of restenosis after percutaneous coronary intervention. The major disadvantage is that patients need to remain on clopidogrel in addition to ASA for at least one year. It takes longer for drug eluting stents to develop an endothelial lining. Drug-eluting stents are therefore more prone to thrombotic occlusion and require a longer period of dual antiplatelet therapy. Dual antiplatelet therapy increases the risk of bleeding. About 25 to 30% of patients on both ASA and clopidogrel will have nuisance bleeding with easy bruising and increased bleeding from cuts; 5% will have internal bleeding; and < 1% will have life-threatening bleeding (such as intracranial bleed or bleeding that necessitates blood transfusions). Bleeding risks are higher if the patient is on warfarin in addition to ASA. Patients who have emergency surgery while on clopidogrel and ASA will bleed more and have a greater requirement for blood transfusions.

Answered by: Dr. Bibiana Cujec

10. Vitamin D Intake

With the suggestion that vitamin D prevents cancers, what are some of the recommendations regarding vitamin D intake?

Submitted by: Charles Lynde, MD, Markham, Ontario

Vitamin D supplementation is proven to be beneficial for osteoporosis and fall prevention. Lately, Vitamin D has been promoted as beneficial for extra-skeletal health, such as cardiovascular disease, immune response, muscle function, mortality, and cancer. However, no randomized control trial (RCT) has shown that Vitamin D supplementation is beneficial for any of the above outcomes. Furthermore, a causal association between poor vitamin D status and nearly all major diseases (cancer, infections, and autoimmune, cardiovascular, and metabolic diseases) has not been proven. As a result, the recommendations for Vitamin D (cholecalciferol = D3) supplementation for possible extraskeletal health for the general population is similar to that for osteoporosis and fall prevention, which is anywhere from 800 to 1,000 IU per day of Vitamin D. In patients with Vitamin D deficiency [25(OH)D < 50 nmol/L], treatment with 50,000 units of vitamin D2 or D3 orally once per week for six to eight weeks, followed by a maintenance dose (*e.g.*, 800 to 1,000 units of vitamin D3 daily) thereafter, is recommended.

Answered by: Dr. Ally Prebtani

11. Managing Diabetes through Diet

How can a patient change his or her diet to help control his or her diabetes mellitus? What should he avoid? What should be consumed?

Submitted by: Sarah Schmidt, MD, Toronto, Ontario

In general, most patients can control their diabetes mellitus better if they follow these simple rules: eat three meals (including breakfast) per day at regular times with healthy snacks in between (*e.g.*, fruits and vegetables); limit sugars and sweets (regular pop, desserts, candies, jam, and honey); limit the amount of high-fat food, such as fried foods, chips, and pastries; and eat more high-fibre foods, such as whole grain breads and cereals, lentils, dried beans and peas, brown rice, and vegetables and fruits. Have a glass of skim or 1% milk to complete your meal. Alcohol can affect blood glucose levels and cause you to gain weight, so it must be consumed in moderation, or eliminated from your diet completely. Include fish, lean meats, low-fat cheeses, eggs, or vegetarian protein choices as part of the meal. All people with diabetes should also receive advice on nutrition from a registered dietitian. Of course, it is important to take into consideration each patient's cultural background with respect to dietary intake. In addition to diet, regular physical activity is important along with medications if necessary.[1]

Reference

1. Canadian Diabetes Association: 2008 Clinical Practice Guidelines. Canadian Diabetes Association Diabetes Care, 2009; 32(7): n.p.

Answered by: Dr. Ally Prebtani

12. Otoliths Causing Vertigo

What is the evidence for otoliths causing vertigo?

Submitted by: Don Pinkson, MD, Guelph, Ontario

There is excellent evidence that otoliths contribute to benign positional paroxysmal vertigo (BPPV). Although the exact mechanism is still partially debated, the presence of otoliths within the semicircular canals (SCC) is implicated in BPPV. Otoliths do not contribute to other causes of vertigo, such as vestibular neuronitis or Ménière's disease.

BPPV presents as a short duration (around 20 seconds) true vertigo, classically stimulated by a change in head position, and it can be associated with nausea and vomiting. Patients can suffer from disequilibrium or a "cloudy" feeling for minutes to hours after the episode; however, the true spinning sensation abates quickly. There are few disorders that cause this pattern of vertigo, and BPPV is by far the most common. The posterior SCC canal is most commonly affected (> 70%), due to its posteroinferior position, and canal stimulation results in a geotropic (towards the downward ear), torsional nystagmus.

Most cases of BPPV are idiopathic. Head trauma is the second most common cause, followed by a long list of otologic conditions. It appears that any insult to the inner ear can predispose an individual to this condition, as evidenced by its association with vestibular neuronitis, otosclerosis, otitis media, Ménière's disease, labyrinthitis, and ear surgery. Establishing the diagnosis of BPPV in this group may be more difficult, but the key symptoms remain the same.

In the absence of other ear diseases, BPPV is not associated with hearing loss or tinnitus, and vertigo does not last longer than one minute. An audiogram should be obtained if any unusual features are present. The Dix-Hallpike maneuver is pathognomonic, although a negative test does not exclude the condition. The remainder of the clinical examination is usually normal. Vestibular function tests are not required for classic cases that respond to initial therapy, but should be considered for recalcitrant symptoms or unusual presentations.

Canalith repositioning physiotherapy, such as the Epley or Semont maneuvers, is the treatment of choice. These therapies have a success rate of around 90%. Given the short duration of symptoms and the common success of these exercises, vestibular suppressant medications should be avoided. Surgical therapy, such as posterior SCC occlusion, is very rarely required. The key to successful management of these patients is educating them about the cause and teaching them repositioning exercises. Patient handouts or online resources (including videos of the maneuvers on YouTube) will help patients perform these exercises at home and keep their symptoms under control.

Answered by: Dr. Ben Dixon

13. Hemochromatosis Incidence

Is the incidence of hemochromatosis on the rise (I seem to diagnose more of it)? And, is ferritin a good enough screening test, especially in women?

Submitted by: Christo Rabie, MD, Calgary, Alberta

Hereditary hemochromatosis (HH) has been well studied by the Hemochromatosis and Iron Overload Study (HEIRS) investigators.[1] The commonly identified mutations occur in the HFE gene. In the HEIRS cohort, approximately 1 in 10 to 15 individuals of Caucasian descent are carriers of one of these abnormal gene mutations, and 1 in 200 to 300 individuals are homozygote or compound heterozygote for the most common gene mutations. There is no known documented evidence that this rate of incidence is on the rise.

Ferritin, a macromolecule that contains thousands of iron atoms, is generally an intracellular storage protein for iron. Approximately 1% of the body's ferritin is soluble in plasma and is in equilibrium with the intracellular storage ferritin. Serum ferritin, albeit an imperfect measure of the body's iron stores, is a noninvasive and cheap test; it is generally a better screening test for iron deficiency than for iron overload. It is a nonspecific test of iron content, as ferritin is an acute phase reactant and may become falsely elevated in the presence of inflammation. A more sensitive, yet still inexpensive and noninvasive, test for iron overload is transferrin saturation (T. sat). This is a measure of the percentage of transferrin molecules, the body's iron transporters, that are bound to iron. No absolute elevation in transferrin saturation is agreed upon as a universal standard; however, levels above 60% in males and 45 to 50% in females should raise suspicion and call for a repeat test. The gold standard to diagnose iron overload is still an invasive liver biopsy.

General population-based screening for HH is not recommended. Clinical features for HH may include a known family history, individuals in their fifth or sixth decade of life who present with darkened (or tanned-appearing) skin, arthritis, type 2 diabetes mellitus, liver function abnormalities or hepatomegaly, and/or cardiomyopathies without other underlying causes. In general, menstruating women who have HH have a delayed onset of iron overload compared to men due to menstrual blood loss. Men and postmenopausal women should have iron indices (T. sat and ferritin) assessed, and, if no underlying cause for elevation can be found (*i.e.*, infections or inflammation), then sending samples for molecular diagnostic testing for mutations in the HFE gene would be reasonable.

Reference

1. Adams PC, Reboussin DM, Barton JC, *et al*: Hemochromatosis and Iron-overload Screening in a Racially Diverse Population. N Engl J Med 2005;352(17):1769–1778.

Answered by: Dr. Cyrus Hsia and Dr. Leonard Minuk

14. Pimecrolimus vs. Tacrolimus

Which is the most effective treatment of eczema — pimecrolimus or tacrolimus?

Submitted by: Larry Bobyn, MD, Kelowna, British Columbia

Pimecrolimus and tacrolimus are nonsteroidal calcineurin inhibitors that have been shown to be effective in treating atopic eczema in randomized controlled trials. Pimecrolimus is available as a 1% cream, and tacrolimus is available as a 0.03% and a 0.1% ointment. They are useful in treating atopic eczema, as they have anti-inflammatory properties without the major side effects of topical corticosteroids (*i.e.,* atrophy and depigmentation). The primary side effect of pimecrolimus cream and tacrolimus ointment is burning or stinging of the skin after topical application.

Pimecrolimus 1% cream is approved for treating mild to moderate atopic eczema in children over two-years-of-age. Tacrolimus is approved for treating moderate to severe atopic eczema with the 0.03% ointment approved for ages 2 to 15 and the 0.1% ointment approved for patients over the age of 15.

Tacrolimus 0.03% ointment and 0.1% ointment are both more effective than 1% pimecrolimus cream in treating atopic dermatitis. In a randomized, controlled, multicentre study lasting six weeks, tacrolimus 0.1% ointment was shown to be more effective and have a faster onset of action than 1% pimecrolimus cream in adults and in pediatric patients with moderate to severe atopic dermatitis. The same results were seen with tacrolimus 0.03% ointment versus 1% pimecrolimus cream for pediatric patients with mild atopic dermatitis. In this study, the safety profiles of tacrolimus and pimecrolimus were shown to be similar.[1]

Reference

1. Paller AS, Lebwohl M, Flesicher AB, *et al*: Tacrolimus Ointment is More Effective than Pimecrolimus Cream with a Similar Safety Profile in the Treatment of Atopic Dermatitis: Results from 3 Randomized, Comparative Studies. J Am Acad Dermatol 2005; 52(5):810–22.

Answered by: Dr. Richard Haber

15. Desensitizing Allergic Individuals

Are there safe and effective means to desensitize allergic individuals with peanut or shellfish anaphylaxis?

Submitted by: William Fair, MD, Vernon, British Columbia

Allergen immunotherapy via the injection route has been used successfully for the treatment of allergic rhinoconjunctivitis and venom hypersensitivity for decades. Despite its efficacy in these settings, this approach has been shown to be unsafe for treatment of food allergy, due to an unacceptably high rate of anaphylactic reactions.[1] Currently, alternatives to subcutaneous injection therapy are being investigated for treatment of food allergy, one of which is oral desensitization.

Desensitization is defined as a change in the threshold dose of ingested food allergen necessary to cause allergic symptoms; this state is dependent upon ongoing food antigen exposure. In contrast, tolerance is the induction of long-term immunologic changes associated with the ability to ingest a food without symptoms and without ongoing therapy. Although fish desensitization has been reported, this has not been explored extensively, and, to my knowledge, shellfish desensitization has not been described in recent literature.[2] Trials involving allergen-specific therapies have involved peanuts, cow's milk, hazelnuts, eggs, and kiwi. These have involved oral, sublingual, and epicutaneous methods of administration, and have shown varying success in increasing the threshold dose tolerated by patients. In addition, immunologic changes that have been demonstrated include reduction in specific IgE, increase in sIgG4, and reduced Th2 cytokine production and basophil/mast cell reactivity, all of which are associated with development of clinical tolerability. Oral immunotherapy appears to be effective in inducing desensitization in most patients, as well as oral tolerance in a subset of patients with food allergy.[3]

These kinds of studies, many of which are ongoing, are very encouraging, but they are all small and very preliminary. However, we are now closer to applying more definitive therapeutic options and providing hope for food allergic patients and families. It should be noted that these approaches are associated with significant risk and at present should only be conducted by experienced investigators in clinical trial centres. Ongoing studies will hopefully move toward broader clinical application in the future.

References
1. Oppenheimer JJ, Nelson HS, Bock SA, *et al*: Treatment of Peanut Allergy with Rush Immunotherapy. J Allergy Clin Immunol 1992; 90(2): 256–262.
2. Patriarca G, Nucera E, Roncallo C, *et al*: Oral Desensitizing Treatment in Food Allergy: Clinical and Immunological Results. Aliment Pharmacol Ther 2003;17(3):459–465.
3. Blumchen K, Ulbricht H, Staden U, *et al*: Oral Peanut Immunotherapy in Children with Peanut Anaphylaxis. J Allergy Clin Immunol 2010; 126(1):83–91.

Answered by: Dr. Tom Gerstner

16. Onset of Celiac Disease Symptoms

Can celiac disease show up later in life, when patients have completely new symptoms? Are people born with it, or can they develop it at any time?

Submitted by: Christine Gibson, MD, Calgary, Alberta

Celiac disease, celiac sprue, or gluten-sensitive enteropathy is a relatively common disease affecting 0.5 to 1% of the North American and European populations. Although it is classically diagnosed in children, it is being increasingly diagnosed in adults, and about 20% of cases are diagnosed in patients over 60 years of age. Some patients, despite being diagnosed in adulthood, have had symptoms for many years predating diagnosis, but many have not.

Celiac disease is an autoimmune condition with a genetic basis, and it is triggered by gluten, an environmental factor. Thus, like other autoimmune conditions, people are born with gluten-sensitivity and, thus, do not develop or outgrow the disease. However, the symptoms associated with gluten-sensitive enteropathy are so varied both in presentation and in severity that many people with the disease are not diagnosed until much later in life.

The classic symptoms of diarrhea and abdominal distension/bloating are absent in approximately half of all patients with celiac disease. Iron-deficiency anemia is now the most common presentation. Patients can also present with evidence of other deficiencies, such as B12, folate, vitamin K, and vitamin D. Nonspecific symptoms, including fatigue, recurrent aphthous stomatitis, fractures, arthralgias, infertility, and psychiatric syndromes, can also be the sole complaint. In children, impaired growth, pubertal delay, rickets, poor dentition, and behavioural issues should alert the physician to consider celiac disease, among other diagnoses.

For patients with associated conditions, such as dermatitis herpetiformis, IgA deficiency, type 1 diabetes, autoimmune thyroid disease, Down's syndrome, IgA nephropathy, microscopic colitis, rheumatoid arthritis, and Sjogren's syndrome, physicians should have a low threshold to test for gluten-sensitive enteropathy.

Resource

1. Farrell RJ, Kelly CP: Celiac Sprue. N Engl J Med 2002; 346(3):180–188.

Answered by: Dr. Robert Bailey and Dr. Carrie Ye

17. Foods to Avoid during Pregnancy

Many newly pregnant patients ask which foods/drinks to avoid during pregnancy. Besides alcohol are there any definite foods to avoid?

Submitted by: Gail Dangoor, MD, Thornhill, Ontario

One of the most important subjects to discuss in pregnancy is how to avoid foodborne illnesses, which can cause maternal disease as well as congenital disease, premature labour, miscarriage, and fetal death. Expecting mothers should wash their hands frequently; only consume meats, fish, poultry, and eggs that are fully cooked; avoid unpasteurized dairy products and fruit/vegetable juices; wash fresh fruits and vegetables thoroughly prior to eating; avoid eating raw sprouts; and wash all surfaces that come in contact with raw fish, meat, and poultry with soap.

Toxoplasmosis can be caused by eating undercooked or cured meats, soil-contaminated fruits and vegetables, and contaminated, unfiltered water.

Listeria is a common low-level contaminant in processed and unprocessed foods; however, hot, cooked foods are not a vehicle. Listeria is most commonly associated with processed meats, hot dogs, soft cheeses, smoked sea food, meat spreads, and pate.

Brucellosis is caused by contaminated foods, such as raw milk, raw meat, or cheeses made from unpasteurized milk.

Dietary restrictions include the avoidance of shark, swordfish, king mackerel, and tilefish, because they may contain high levels of mercury. The consumption of seafood low in mercury (shrimp, canned light tuna, salmon, pollock, catfish) should be limited to two meals a week. Albacore tuna has higher levels of mercury and should be limited to one meal of the total.[1]

Herbal medicines should be avoided in pregnancy, as there is no control on the strength or purity, and there have been several documented cases of potential harmful effects on pregnancy.[2]

Only observational studies suggest some negative effect of caffeine on pregnancy, but it is considered prudent to limit caffeine consumption to less than 200 mg per day.

There is no evidence that artificial sweeteners increase the risk of birth defects, and most individuals consume much less than the "Acceptable Daily Intake" suggested by the FDA.

A balanced, healthy diet based on the Canadian Nutritional Guidelines is recommended with appropriate vitamin and mineral supplementation.

References

1. Food Safety: Product Specific Information. United States Federal Food and Drug Administration [Internet]. http://www.fda.gov/Food/FoodSafety/Product-SpecificInformation/default.htm. Accessed May 10, 2011.
2. Ernst E: Herbal Medicinal Products During Pregnancy: Are They Safe? BJOG 2002;109(3):227–235.

Answered by: Dr. Victoria Davis

18. Chest X-rays for Pneumonia Patients

In a patient with pneumonia, diagnosed with chest x-ray, how long after treatment should chest x-ray be repeated?

Submitted by: Mark Krieger, MD, Toronto, Ontario

The necessity and timing of performing a follow-up chest radiograph (CXR) in the management of community-acquired pneumonia depends on the clinical context. Patients who fail to respond clinically (*e.g.,* no improvement in cough, fever, tachypnea, hypoxemia, or leukocyte count) after 48 to 72 hours of treatment with antimicrobials warrant a follow-up CXR. Among patients that do respond clinically to appropriate treatment of pneumonia, only those who are at increased risk for lung malignancy require follow-up CXR (*e.g.,* smoking history, family history of lung cancer, age > 50 years, worrisome features on initial CXR).

The timing of a follow-up CXR, in the setting of a good clinical response to treatment, is influenced by the presence of factors associated with slow radiographic resolution (see Table 1). Most individuals without risk factors for slow resolution of pneumonia will show clearing on CXR after four to six weeks. However, individuals with risk factors may take much longer to clear radiographically — 12 weeks or more.

Table 1
Risk Factors for Slow Radiographic Response in Pneumonia

- Older age
- Underlying chronic lung disease
- Immunosuppression
- Increased severity of pneumonia
- Inadequate antimicrobial therapy
- Features on chest radiograph (*e.g.*, multilobar involvement, cavitary disease, pleural effusion, atelectasis)

Resource

1. Mandell LA, Wunderink RG, Anzueto A, *et al*: Infectious Disease Society of America/American Thoracic Society Consensus Guidelines on Management of Community-acquired Pneumonia in Adults. Clin Inf Dis 2007; 44(Suppl 2): S27–S72.

Answered by: Dr. Paul Hernandez

19. Treatment of Neuropathic Pain

Please discuss current treatment options for neuropathic pain.

Submitted by: V. Dunraj, MD, Toronto, Ontario

The treatment for neuropathic pain is mainly symptomatic. There are multiple pharmacological agents that can be used to treat neuropathic pain. The following are commonly used agents:

- *Tricyclic Antidepressants*: The pain-relieving effect of these agents is independent of their antidepressant effect. Amitriptyline is one of the commonly used medications. It can be started as low as 10 mg at bedtime and increased gradualy. Side effects may include drowsiness, increased appetite, constipation, urinary retention, blurred vision, and dry mouth. Elderly patients may experience confusion and find it difficult to tolerate. Other tricyclic antidepressants include imipramine, desipramine, nortriptyline, and clomipramine.
- *Gabapentin:* The exact mechanism of action of gabapentin in neuropathic pain is unknown. It can be started at 100 mg three times daily and slowly increased up to 600 mg three times daily, or even higher if necessary. Side effects may include dizziness, and drowsiness at high doses.
- *Pregabalin*: The exact mechanism of action of pregabalin in neuropathic pain also remains unknown. It can be started at 25 mg twice daily and slowly increased up to 150 mg twice daily. Side effects may include dizziness and sleepiness.
- *Capsaicin*: Capsaicin can be used topically and acts on the C-nociceptor peripheral fibers. It causes depletion of substance P in peripheral fibers. It may cause local skin irritation in some cases.
- *Anticonvulsants*: These agents may have some analgesic effect in neuropathic pain. Initial reports of these analgesic effects were noted while patients used phenytoin in 1942. Several reports indicate successful use of anticonvulsants, including phenytoin and carbamazepine, in treatment. Carbamazepine and lamotrigine are other effective anticonvulsants. Carbamazepine is the drug of choice in trigeminal neuralgia, and may be used to relieve pain due to diabetic neuropathy; it is the most frequently used anticonvulsant in treatment of neuropathic pain.

Other agents, such as baclofen, ketamine, and clonidine, and procedures, such as nerve blocks, may have a partial role in the treatment of neuropathic pain.

Use of other pharmacological agents to treat neuropathic pain is not fully supported by appropriate clinical trials. Thus, not one pharmacological intervention is guaranteed to be completely successful. Those patients who fail to respond to these pharmacological agents may use other modalities of treatment, such as behaviour modification and fostering of coping skills. The successful management of the patient with neuropathic pain still remains a challenge.

Answered by: Dr. Abdul Qayyum Rana

20. When to Stop Bisphosphonates

When should you stop bisphosphonates in post menopausal women?

Submitted by: Sylvie Gill, MD, Sorel-Tracy, Québec

There is no clear consensus on how long patients should be treated with bisphosphonates. The most widely referred to study that helps to answer this question is the FLEX trial, which was an extension of the FIT trial.[1] Women who received alendronate for five years in the FIT trial were randomized to continue alendronate for another five years or to take placebo in the FLEX trial. Note that women at the highest risk for fracture were excluded in this trial. At 10 years, patients who took placebo had a gradual decline in their bone mass density (BMD), as well as a gradual rise in their bone turnover markers; however, their BMD remained higher than the level 10 years earlier. Rate of nonvertebral fracture was not significantly different, but there was a slightly higher risk of clinically detected vertebral fractures (5.3 and 2.4% for placebo and alendronate respectively).

From this information, stopping alendronate after five years might be reasonable for low risk women based on their assessment of fracture risk as well as the clinical judgement of the physician. Since high risk patients were excluded from the FLEX trial, continuing alendronate in this population is recommended; however, there is no data beyond 10 years.

Current Canadian guidelines state that "there is little evidence to support any recommendation regarding duration of therapy or the use of drug holidays."[2] They recommend that patients at "high risk for fracture should continue osteoporosis therapy without a drug holiday."

Reference

1. Watts NB, Chines A, Olszynski WP, *et al*: Fracture Risk Remains Reduced One Year After Discontinuation of Risedronate. Osteoporos Int 2008; 19(3):365–372.
2. Papaioannou A, Morin S, Cheung AM, *et al*: 2010 Clinical Practice Guidelines for the Diagnosis and Management of Osteoporosis in Canada: Summary. CMAJ 2010; 182(17):1864–1873.

Answered by: Dr. Michael Starr

21. Clues to Diagnose Bipolarity

In a depressed person, what clues can lead to a diagnosis of bipolarity? Can a trial of SSRI lead to a manic episode?

Submitted by: **Waguin Tannous, MD,** Montréal, Québec

Each of the following features, particularly when they exist in combination, may be predictive of bipolar disorder:

- Onset of depressive or hypomanic/manic symptoms at an early age
- Psychotic depression before 25-years-of-age
- Postpartum depression, especially one with psychotic features
- Rapid onset and offset of depressive episodes of short duration (less than three months)
- Recurrent depression (more than five episodes)
- Depression with marked psychomotor retardation
- Atypical features (reverse vegetative signs)
- Seasonality
- Bipolar family history
- Trait mood lability (cyclothymia)
- Hyperthymic temperament

A trial of SSRI can lead to a manic or hypomanic switch if given to a bipolar disorder patient with any of the following:

- Prior history of switches to mania on antidepressant medications
- Rapid cycling history
- Onset of depression at a young age, particularly a prepubertal onset of depression
- Mixed depression with racing thoughts

Resource

1. Chapter 13: Mood Disorders. In: Kaplan & Sadock's Comprehensive Textbook of Psychiatry. 9th edition. Lippincott, Williams, & Wilkins, Philidelphia, 2009, 1629–1839.

Answered by: **Dr. Hany Bissada**

22. Significance of Endometrial Cells on a Pap Smear

What is the significance of endometrial cells on a Pap?

Submitted by: Maria Yu, MD, Ajax, Ontario

Endometrial cells on a Pap smear in women over 40-years-old may reflect physiologic shedding (especially in the first 12 days of the menstrual cycle) or shedding in response to a pathological process. The cells are reported so the clinician can determine their significance in individual patients.

Large reviews of benign-appearing endometrial cells on cervical cytology in women over 40 have reported that up to 16% can be associated with significant endometrial pathology (hyperplasia or carcinoma). Among women with significant pathology, 79% had abnormal bleeding. Therefore, if symptoms of endometrial cancer are present (abnormal uterine bleeding), the patient should undergo endometrial sampling regardless of menopausal status.

In premenopausal women without abnormal bleeding, benign-appearing endometrial cells are rarely associated with significant pathology, and no further workup is indicated. However, endometrial sampling can be offered to asymptomatic women with benign-appearing endometrial cells who are at risk for endometrial cancer (personal or family history of breast, colon, or endometrial cancer; tamoxifen use; chronic anovulation; obesity; estrogen therapy; prior endometrial hyperplasia; diabetes). Endometrial sampling is preferable over an ultrasound, as a negative ultrasound does not rule out pathology. Dx

Resource

1. Canfell K, Kang YJ, Clements M, *et al*: Normal Endometrial Cells in Cervical Cytology: Systematic Review of Prevalence and Relation to Significant Endometrial Pathology. J Med Screen 2008;15(4): 188–198.
2. Beal HN, Stone J, Beckmann MJ, *et al*: Endometrial Cells Identified in Cervical Cytology in Women > or = 40 Years of Age: Criteria for Appropriate Endometrial Evaluation. Am J Obstet Gynecol 2007; 196(6):568.

Answered by: Dr. Victoria Davis