Experts on Call

Answers to your questions from our medical experts

1. SSRI Withdrawal

Why do some patients experience withdrawal symptoms when SSRIs are discontinued after one or two years?

Submitted by: Ernest McCrank, MD, Calgary, Alberta

There is a well recognized withdrawal or discontinuation syndrome that is caused by the abrupt cessation of short half-life SSRIs. The incidence of this syndrome is inversely proportional to the half-life of the SSRI that is being abruptly stopped. The exact mechanism causing the withdrawal syndrome is not yet clearly understood. However, it is important to advise patients to avoid abruptly stopping this class of drug, as it happens often when patients skip or forget to take the drug for two to three days. If it is decided that the patient should discontinue an SSRI, it should be done gradually, over the course of weeks, rather than days. If the patient still experiences withdrawal symptoms after the last dose of the SSRI is stopped, then prescribing another SSRI with a longer half-life, such as fluoxetine at 20 mg/day for a couple of weeks, may alleviate the withdrawal symptoms.[1]

Reference
1. Kelsey JE: Serotonin Reuptake Inhibitors. In: Kaplan & Sadock Comprehensive Textbook of Psychiatry. 8th edition. Lippincott Williams & Wilkins, Philadelphia, 2004, 2890.

Answered by: Dr. Hany Bissada

2. Screening for Cushing's Syndrome

What is the best first test to screen for Cushing's syndrome?

Submitted by: Johanne Rioux, MD, Lambert, Québec

The first step is to make sure the patient does not have Pseudo-Cushing's (severe obesity, poorly controlled diabetes mellitus, alcoholism, or severe depression), since these conditions can give false positive biochemical results. Currently, the two best screening tests for Cushing's are the 1 mg overnight dexamethasone suppression test (DST) and the 24 hour urine free cortisol with a corresponding 24 hour urine creatinine to ensure adequate collection. The 1 mg overnight DST is performed by giving the patient 1 mg p.o. dexamethasone at 11pm with an 8am cortisol the following day, which normally should be < 50 nM. These tests are not 100% accurate and can be affected by renal function, other drugs, Pseudo-Cushing's, and acute illnesses, and all of these possibilities need to be taken into account. If either of these tests is positive, further confirmatory tests need to be done.

Answered by: Dr. Ally Prebtani

3. Giant Cell Myocarditis

Can you tell me what I need to know about giant cell myocarditis? Is it related to giant cell arteritis? How do you diagnose and treat the condition? Who is at risk?

Submitted by: Monique Moreau, MD, Alliston, Ontario

There is no clinical relationship between giant cell arteritis and giant cell myocarditis despite a similar pathologic abnormality. Giant cell myocarditis is a fulminant myocarditis often associated with cardiogenic shock, ventricular arrhythmias, and heart block. It typically affects young patients under the age of 55. It is less common, and more serious, than viral or lymphocytic myocarditis. Many patients with giant cell myocarditis require mechanical support and cardiac transplantation or die within a short period of time. Diagnosis is made with an endomyocardial biopsy, which shows extensive myocyte necrosis with a mixed inflammatory infiltrate of lymphocytes, histiocytes, and multinucleated "giant cells" in the absence of sarcoid-like granuloma. Giant cell myocarditis is probably secondary to an autoimmune reaction to myocardial proteins, and it may respond to immunosuppressive treatment.

Giant cell arteritis (temporal arteritis) is a medium to large vessel chronic vasculitis, with predilection for external carotid artery involvement in older patients (> 55 years of age). It is often associated with polymyalgia rheumatica. Symptoms include headaches, jaw claudication, fever and anemia, and monocular blindness. Patients have a high erythrocyte sedimentation rate and C-reactive protein. There may be tenderness on palpation of the temporal arteries. Diagnosis is based on temporal artery biopsy, and there is an excellent response to high dose steroids.

Both conditions are probably the result of an autoimmune response, which in one case is directed against myocytes and in the other case is directed against arterial walls. The common pathologic finding is giant cells upon biopsy. These large, multinucleated cells, also called Langhans' giant cells, are formed by the fusion of macrophages. Giant cells are also found in granulomatous diseases, including tuberculosis, syphilis, sarcoidosis, and fungal infections.

Answered by: Dr. Bibiana Cujec

4. Zoophilic Dermatophytes

What kind of fungal skin infections may a farmer working with cows get? What treatment do you suggest before getting the results of the culture?

Submitted by: Céline Bordeleau, MD, Trois Pistoles, Quebec

The most common zoophilic dermatophytes that cause "cattle ring worm" and are transmissible to humans are *Trichophyton verrucosum* and *Trichophyton mentagrophytes*. *Trichophyton verrucosum* is the species that is most frequently transmitted to humans. These fungi can produce typical tinea corporis lesions in humans, but they are also capable of producing kerion reactions, because zoophilic fungi can induce a marked inflammatory response to the fungal hyphae. If a zoophilic dermatophyte infection is suspected in a farmer, a scraping must be taken for a KOH test and a fungal culture to make a definite diagnosis. As these are zoophilic fungi, they would not be transmissible by human to human spread. After obtaining specimens for KOH and fungal culture, one could then treat the farmer with topical terbinafine cream q.d. if he or she is symptomatic. A positive KOH would be very suggestive of the diagnosis, but only a positive fungal culture will be definitive. If a kerion was suspected, it may be more difficult to confirm the diagnosis because of the marked inflammation, but scrapings must still be taken to try to confirm the diagnosis. Kerion reactions would require oral therapy, usually with oral terbinafine 250 mg q.d. for three to four weeks, and occasionally oral prednisone would need to be added to reduce the inflammatory response and to try to minimize scarring.

Answered by: Dr. Richard Haber

5. NASH Treatment

What is new in Non-alcoholic steatohepatitis (NASH) treatment?

Submitted by: Elena Nelson, MD, Surrey, British Columbia

The mainstay of treatment of NASH is to lose weight by diet and exercise. There is recent evidence to suggest that vigorous exercise is more effective than moderate exercise.[1] There is also some evidence that Vitamin E 800 IU daily can improve the histologic appearance of hepatic steatosis and improve AST and ALT levels.[2]

References
1. Kistler KD, Brunt EM, Clark JM, *et al*: Physical Activity Recommendations, Exercise Intensity, and Histological Severity of Nonalcoholic Fatty Liver Disease. Am J Gastroenterol 2011; 106(3):460–68.
2. Sanyal AJ, Chalasani N, Kowdley Kv, et al: N Engl J Med 2010;362(18):1675–85.

Answered by: Dr. Richmond Sy

6. Parkinsons and Coenzyme-Q10

What advice do you give to Parkinson patients regarding the use of coenzyme-Q10 and the dosage?

Submitted by: Judy A. Dercksen, MD, Quesnel, British Columbia

In several studies of coenzyme-Q10, at various dosages, no significant beneficial effect on Parkinson's disease (PD) symptoms was observed. One four week study with coenzyme-Q10 at a dosage of 360 mg reported some improvement of Parkinson's disease symptoms. In another study, coenzyme-Q10 was found to be safe and well tolerated at dosages of up to 1200 mg daily. Less disability developed in subjects taking coenzyme-Q10 as compared to placebo. The benefit was greatest at the highest dosage. Coenzyme-Q10 was reported to slow the progressive deterioration of function in PD; however, the sample size was small and these results needed to be confirmed in a larger study.

Based upon multiple conflicting reports, there is no current consensus about the routine use of coenzyme-Q10 in Parkinson's disease management.

Suggested Reading
1. Shults CW, Beal MF, Fontaine D, *et al*: Absorption, Tolerability, and Effects on Mitochondrial Activity of Oral Coenzyme Q10 in Parkinsonian Patients. Neurology 1998;50(3):793–5.
2. Shults CW, Oakes D, Kieburtz K, *et al*: Parkinson Study Group. Effects of Coenzyme Q10 in Early Parkinson Disease: Evidence of Slowing of the Functional Decline. Arch Neurol. 2002;59(10):1541–50.

Answered by: Dr. Abdul Qayyum Rana

7. Prescribing for Mild Cognitive Impairment

Upon diagnosing mild cognitive impairment, would it be appropriate to prescribe cholinesterase inhibitors, since roughly 20% of patients progress to having dementia in 12 months?

Submitted by: Rajen Ramgoolan, MD, Winnipeg, Manitoba

The cholinesterase inhibitors rivastigmine and galantamine have been demonstrated to be effective in outpatients with mild to moderate Alzheimer's disease (MMSE scores between 10 and 26). Some experts believe that cognitive efficacy is also apparent in patients with milder cognitive impairment, but very few studies have been done in patients with mild Alzheimer's disease or mild cognitive impairment. All treatments should be started at the lowest possible dose and be titrated gradually so that cholinergic adverse effects are minimized. Renal impairment and hepatic dysfunction can also affect dosing schedules.

Resource

1. Schneider, LS: Antidimentia Drugs. In: Howes, SE (ed.): *Kaplan & Sadock's Comprehensive Textbook of Psychiatry*. 9th edition. Lippincott Williams & Wilkins, Philadelphia, 2009, 4119-4129.

Answered by: Dr. Hany Bissada

8. Treating Headaches in Pregnancy

How do you treat chronic daily headaches in pregnancy?

Submitted by: J. Thomas, MD, Clearwater, British Columbia

Headaches occur in over 80% of women during their child-bearing years and, therefore, are often present during pregnancy. Unfortunately, no large trials of headache therapy in pregnant women are available to provide data on which to base therapeutic recommendations. The major consideration is to "do no harm," since a history of headaches does not appear to adversely affect pregnancy. Those individuals who continue to have headaches after several days of acetaminophen, acetaminophen plus metoclopramide, acetaminophen-codeine, acetaminophen-caffeine-butalbital (acetaminophen-caffeine-butalbital, fioricet, one to two tablets every four hours, not to exceed six tablets per day) should be assessed for provoking factors.

High doses of caffeine in early pregnancy have been associated with an increased risk of miscarriage, and prolonged use of codeine or barbiturates near term can cause neonatal withdrawal, but none are associated with an increased risk of congenital anomalies. Prolonged use of barbiturates can cause vitamin K responsive bleeding. Non-steroidal anti-inflammatory drugs should be avoided in the third trimester due to concerns with premature closure of the ductus. For moderate to severe symptoms, triptans may be considered (sumatriptan, rizatriptan, zolmitriptan, and naratriptan).

Ergotamine is absolutely contraindicated in pregnancy.

Beta-blockers (atenolol, metoprplol, and propranolol) may be considered for prophylaxis, but may be associated with fetal growth restriction, neonatal transient bradicardia, respiratory depression, hyperbilirubinemia, and hypoglycemia. Low dose antidepressants may also be considered for prophylaxis.

If the patient is not responding to these measures, the best suggestion is to consult a neurologist.

References
1. Menon R, Bushnell CD: Headache and Pregnancy. Neurologist 2008;14(2):108–19
2. Lucas S: Medication Use in the Treatment of Migraine During Pregnancy and Lactation. Curr Pain Headache Rep 2009;13(5):392–8.

Answered by: Dr. Victoria Davis

9. Oral Allergy Syndrome

What is the management and treatment of oral allergy syndrome?

Submitted by: D. Grant Kirk, MD, Stellarton, Nova Scotia

Oral allergy syndrome (OAS), or food pollinosis syndrome, is typified by local oral mucosal allergic reaction to various fresh fruits and vegetables, which cross react with common pollens (*e.g.,* tree and grass pollens). Once degraded in the stomach, these foods lose their allergenicity. The structural breakdown of these foods also occurs upon cooking. This is distinct from allergens like peanuts or fish, which are stable against heating and quick breakdown via stomach acids, and whose allergenic epitope is more likely a linear amino acid sequence, rather than a more easily degraded secondary or tertiary structured allergen. Thus, these patients may ingest cooked or processed forms of these foods (*e.g.,* apple pie vs. raw apples).

Common examples of this form of allergy include tree pollen allergy with apples, pears, peaches, and cherries and weed pollen allergy associated with melons (watermelon, cantaloupe, honeydew). Strictly speaking, adrenaline autoinjectors are not required for most patients with OAS. However, the most important factor in determining risk is the history of the reaction (*i.e.*, severity), and an epinephrine autoinjector should be prescribed in patients where more than just mild oral symptoms are reported. Consultation with an allergist would be useful to help define these risks, and, through testing, to identify the relevant food and aeroallergen relationships.

Answered by: Dr. Tom Gerstner

10. Optimizing Coagulation

A cancer patient on nadraparin (for DVT) develops new DVT and then PE, but bleeding is prolonged upon venous puncture. INR is normal. How can coagulation be optimized?

Submitted by: Stephen Ashwell, MD, Dawson Creek, British Columbia

Venous thromboembolic events (VTE) including deep vein thrombosis (DVT) and pulmonary embolism (PE) are relatively common events in cancer patients, occurring with a four-fold increased frequency compared to the general population. Most patients developing VTE in the setting of malignancy are now treated with six months of low molecular weight heparin (LMWH), due to favourable results seen in the CLOT study (which demonstrated reduced risk of recurrent VTE events when compared to vitamin K antagonist therapy).[1] Patients in the CLOT study treated with therapeutic doses of LMWH still had a 9% risk of recurrent VTE. There is little evidence in the literature to guide treatment of these patients, and no randomized control trials exist. Our practice is to administer supra-therapeutic doses of LMWH (*i.e.,* 120% dose) in these cases based on a retrospective study by Carrier, Le Gal, Cho, et al.[2] In that study, this strategy resulted in a low rate of second recurrence of 8.6% with few bleeding complications. We try to avoid the use of inferior vena cava (IVC) filters in these patients unless there is a contraindication to anticoagulation therapy (*i.e.*, bleeding) as IVC filters are associated with a high risk of recurrent VTE events as well as complications relating to the device itself.

References
1. Lee AY, Levine MN, Baker RI, *et al*: Low-molecular-weight Heparin versus a Coumarin for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer. N Engl J Med 2003; 349(2): 146–53.
2. Carrier M, Le Gal G, Cho R, *et al*: Dose Escalation of Low Molecular Weight Heparin to Manage Recurrent Venous Thromboembolic Events Despite Systemic Anticoagulation in Cancer Patients. J Thromb Haemost 2009; 7(5): 760–65.

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

11. Dopamine Agonist Therapy

How long should dopamine agonist therapy (cabergoline, bromocriptine) be continued in a middle-aged woman with hyperprolactinemia?

Submitted by: Anonymous

There have been several studies looking at this question. After one to two years of treatment with dopamine agonist therapy, tapering treatment with the goal of withdrawing therapy may be considered if the dose is very low, the patient is asymptomatic, the prolactin is normal, and the MRI shows a small or nonvisible tumour.

Despite withdrawl, these patients still need ongoing, periodic clinical, biochemical, and radiographic follow-up.

Answered by: Dr. Ally Prebtani

12. Pacemaker Indications

Is a pacemaker indicated for an isolated asymptomatic short run of bradycardia?

Submitted by: B. Leonard Chandrarajan, MD, Kingston, Ontario

A permanent pacemaker is generally not indicated in patients who do not have symptoms of hypoperfusion (syncope, presyncope, fatigue) associated with bradyarrhythmias. However, a pacemaker would generally be recommended in patients with high grade AV block (Mobitz type 2 second degree AV block or third degree AV block) with a slow ventricular escape rhythm (<40 bpm), even in the absence of symptoms. These bradyarrhythmias indicate significant conduction system disease and risk for syncope.

Answered by: Dr. Bibiana Cujec

13. Diagnosing Secondary Amenorrhea

Do you have a simple approach to diagnose secondary amenorrhea in premenopausal women (non-pregnant)?

Submitted by: Fawzi Mankal, MD, Ottawa, Ontario

Secondary amenorrhea is the absence of menses for six months. Excluding pregnancy, the most common causes of secondary amenorrhea are ovarian disease, hypothalamic dysfunction, pituitary disease, and uterine disease. A history and physical will usually point to the diagnosis: how long without any bleeding, including spotting; has there been weight gain/loss, acne or hair growth; amount of exercise; any new stressors; are there hot flushes; any uterine surgery; any change of vision; and any chronic illnesses. Blood tests include thyroid function, prolactin, luteinizing hormone (LH), and follicle stimulating hormone (FSH). Androgen evaluation is rarely needed unless there are significant signs of hyperandrogenism. Estrogen status can be assessed by a progesterone withdrawal test (medroxyprogesterone 10 mg or prometrium 200 mg p.o. o.d. for ten days). Ovarian disorders would include ovarian failure (premature menopause if < 40 years old) and polycystic ovary syndrome (PCOS). In the former the LH and FSH will be elevated, whereas in the latter the FSH is usually normal with the LH twice the value of FSH. PCOS is usually diagnosed by history and physical exam to exclude other disorders (thyroid disease or hyperprolactinemia). In hypothalamic dysfunction, the LH and FSH are usually low to normal and may stem from low weight, obesity, excessive exercise (ballet dancers, Olympic athletes, long distance runners), and chronic illness. Pituitary disorders that could cause amenorrhea are thyroid disease and hyperprolactinemia. If the progesterone withdrawal test is positive (bleeding), then the woman has sufficient estrogen and a patent outflow tract. If all blood tests are normal, the medroxyprogesterone withdrawal is negative, and there has been a history of uterine infection or post partum dilatation and curettage, then Asherman's syndrome (intrauterine adhesions) should be considered; this can be diagnosed by hysterosonogram.[1]

Reference

1. Practice Committee of the American Society for Reproductive Medicine. Current Evaluation of Amenorrhea. Fert Steril 2006;86 (5s1):s148–55

Answered by: Dr. Victoria Davis

14. PDE4 Manipulators

What is the role of PDE4 manipulators in the management of COPD?

Submitted by: Prakash Patel, MD, Regina, Saskatchewan

Chronic obstructive pulmonary disease (COPD) is an inflammatory lung disease associated with symptoms of dyspnea, cough, sputum production, exercise intolerance, recurrent exacerbations, expiratory airflow limitation and hyperinflation, and increased mortality. Phosphodiestaerase-4 (PDE4) inhibitors are a novel class of anti-inflammatory drugs that provide a new treatment option in COPD pharmacotherapy. Currently, the only available PDE4 inhibitor is roflumilast, a once daily, oral medication. Roflumilast has been shown in clinical studies to reduce markers of airway inflammation, modestly improve lung function, and significantly reduce rates of moderate to severe exacerbations.[1-3] Unlike methylxanthines, which are nonselective phosphodiesterase inhibitors, there is no need to monitor plasma levels and avoid drug interactions. Side-effects of roflumilast include gastrointestinal intolerance, headache, and weight loss. PDE4 inhibitors should be considered in the management of patients with moderate to severe COPD who continue to experience exacerbations in spite of the regular use of inhaled, long-acting bronchodilators.

Resources

1. Calverley PMA, Rabe KF, Goehring U-M, *et al*: Roflumilast in Symptomatic Chronic Obstructive Pulmonary Disease: Two Randomized Clinical Trials. Lancet 2009; 374 (9691):685–94.
2. Fabbri LM, Calverley PMA, Izquierdo-Alonso JL, *et al*: Roflumilast in Moderate-to-severe Chronic Obstructive Pulmonary Disease Treated with Longacting Bronchodilators: Two Randomized Clinical Trials. Lancet 2009; 374(9691):695–703.
3. Boswel-Smith V, Cazzola M, Page CP: Are Phosphodiesterase 4 Inhibitors Just More Theophylline? J Allergy Clin Immonol 2006; 117(6):1237–43.

Answered by: Dr. Paul Hernandez

15. Immediate Recommendations for Stroke Victims

What are the immediate recommendations for a stroke victim while waiting for ambulance personnel?

Submitted by: Anonymous

A stroke victim, while waiting for the ambulance personnel, should try to relax and take slow, deep breaths, which can help them to calm down. Patients should keep themselves in the lying down position, as the risk of fall increases if they are standing, which can lead to injury. Covering themselves with a blanket may help to keep the body warm and prevent shock.

A stroke victim should not eat or drink anything while waiting for the ambulance to arrive, as stroke may cause the inability to swallow and the patient may aspirate. They should not take aspirin, because until the CT scan is done, it is not known what type of stroke has occurred (*i.e.,* ischemic or hemorrhagic).

Answered by:
Dr. Abdul Qayyum Rana

16. 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 which 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 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