Experts on Call

Answers to your questions from our medical experts

1. Mortality and Morbidity of Renal Dialysis

Please discuss the mortality and morbidity of renal dialysis.

Submitted by: Alice Lai, MD, Toronto, Ontario

The Canadian Organ Replacement Registry (CORR) records key quality indicators for dialysis and renal transplantation patients in Canada. The unadjusted yearly mortality rates for patients on dialysis in Canada range from 9% to 10%. This risk increases based on age (15% to 30% per year mortality rate > 65-years-of-age) and the presence of diabetes (12% to 15% per year mortality). The five year mortality rates for dialysis are comparable to many cancers including breast, colorectal and lymphoma. The mortality from dialysis therapies are high but often underappreciated are the limitations on quality of life imposed by dialysis. Health-related quality of life surveys show dialysis patients have symptom burdens similar to cancer patients (*i.e.*, have higher rates of depression, uncontrolled pain and sexual dysfunction).

Resources
1. 2007 CORR Report - Treatment of End-Stage Organ Failure in Canada 1996 to 2005.
2. Weisbord SD, Fried LF, Arnold RM, et al: Prevalence, Severity, And Importance Of Physical And Emotional Symptoms In Chronic Hemodialysis Patients. J Am Soc Nephrol 2005; 16(8):2487-94.
3. Davison SN, Jhangri GS: The Impact Of Chronic Pain On Depression, Sleep, And The Desire To Withdraw From Dialysis In Hemodialysis Patients. J Pain Symptom Manage 2005; 30(5): 465-73.

Answered by: Dr. Manish Sood

2. Resistant Head Lice

How do you treat resistant head lice (permethrin x 3), if malathion is not useable?

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

The emergence of pediculosis capitis resistant to pyrethroids in North America has made treatment of head lice more challenging.

Malathion shampoo, which is the most ovicidal and effective chemical pediculicide, is not available in Canada.

Resultz™ is a new treatment for head lice that is available OTC in Canada and is safe to use in children and adults. It contains 50% isopropyl myristate and works by dissolving the waxy coating that covers the exoskeleton of the head louse, resulting in dehydration and death. Because it has a mechanical mode of action, resistance is unlikely to develop. As it is not ovicidal, it should be repeated in one week to kill any lice that have hatched from eggs since the first treatment.

Resource
1. Kaul N, Palma KG, Silagy SS, et al: North American Efficacy And Safety Of A Novel Pediculicide Rinse, Isopropyl Myristate 50% (Resultz). J Cutan Med Surg 2007; 11(5):161-7.

Answered by: Dr. Richard Haber

3. Bipolar Disorder Medications During Pregnancy

What medications do you recommend to use for bipolar disorder during pregnancy?

Submitted by: Reynald Gilbert, MD, Lac-Etchemin, Quebec

Practically, all psychotropic medications cross the placenta, however, for obvious ethical reasons, no randomized studies with placebo have examined this topic and consequently, the information available comes from case studies, retrospective studies and animal studies.

Organogenesis takes place over the course of the first 12 weeks following conception. During these three months, each organ is vulnerable to the teratogenic effects of any prescribed medication. The following are important key points to keep in mind when prescribing a psychotropic medication to a bipolar pregnant patient:

- The prescription of lithium, valproate and carbamazepine should be avoided during the first trimester of pregnancy
- When the patient becomes pregnant while she is being treated with a mood stabilizer, the risks and benefits of the treatment must be carefully evaluated, keeping in mind, the number and severity of past episodes and the response to treatment in the patient's history
- For mild to moderate forms of bipolar disorder (fewer episodes, prolonged period of mood stability between episodes and good support network), the advice is gradual decrease and then discontinuation as soon as the pregnancy is detected. Also, it is recommended to avoid treatment with psychotropic medications during the first trimester as much as possible
- For severe forms of bipolar disorder (frequent hospitalizations, several thymic episodes per year, rapid relapse after discontinuation of medication), the advice is to evaluate the risks/benefits of continuing treatment during the first trimester and during the entire pregnancy
- The information available concerning the mood stabilizers topiramate and gabapentin is still very limited and their use is not recommended during pregnancy. Regarding the use of lamotrigine, Morrow, *et al* (2006) reported about a large pregnancy register in which lamotrigine at doses > 200 mg q.d. was significantly responsible for an increase rate of major malformations
- For the classic antipsychotic medications, a meta-analysis suggested an increased risk of malformations when the fetus is exposed to low potency neuroleptics such as chlorpromazine during the first trimester. In practice, if the prescription of a neuroleptic is required, haloperidol or fluphenazine should be preferred. Regarding second-generation antipsychotics, data collected so far show a higher (10%) evidence of low birth weight at delivery compared to control (2%) and an increased frequency of spontaneous abortion (14.5% vs. 8.6%). However, no increased rate of major malformations was reported
- Regarding selective serotonin reuptake inhibitors (SSRIs), data collected so far do not show any increased risk, except for paroxetine which has a high risk of causing cardiac malformations as a result of exposure during the first trimester. Therefore, when prescribing an SSRI, it is recommended to avoid the use of paroxetine during pregnancy or in women wishing to become pregnant
- No significant teratogenic effects have been found to date for tricyclic antidepressants and preliminary data revealed no advanced long-term neurobehavioural effects from *in utero* exposure

Resource

1. Aubry JM, Ferrero F, Schaad N, et al: *Pharmacotherapy of Bipolar Disorders.* John Wiley & Sons, Ltd., West Sussex, England, 2007, pp.1-296.

Answered by: Dr. Hany Bissada

4. Treating Osteopenia with Bone Resorption Medications

What evidence suggests that treating osteopenia with bone resorption medications is clearly superior to using calcium, lifestyle and exercise?

Submitted by: Peter Kujtan, MD, Mississauga, Ontario

It has now become clear that BMD is only one of several factors that contribute to a patient's risk of fracture.

The Osteoporosis Society of Canada guidelines have suggested that BMD reports include a 10-year fracture risk to assist the clinician in determining the need for pharmacotherapy beyond conservative measures such as adequate calcium, vitamin D and exercise.

There are a number of clinical factors that contribute to this fracture risk calculation. Age, previous history of a fragility fracture (after age 40) and the systemic use of glucocorticoids for more than three months are among the most important risk factors that may move a patient into a higher risk category regardless of BMD.

The presence of any high-risk feature, such as glucocorticoid use, increases risk categorization to the next level (*i.e.*, moderate category becomes high-risk category). Table 1 can help the clinician decide which patients may benefit from bisphosphonate therapy and shows that many osteopenic women without significant risk factors could be satisfactorily managed conservatively with exercise and adequate calcium and vitamin D.

Answered by: Dr. Michael Starr

Table 1

10-year risk for women

Age	Low < 10%	Moderate 10%-20%	High > 20%
50	> -2.3	-2.2 to -3.9	< -3.9
55	> -1.9	1.9 to -3.4	< -3.4
60	> -1.4	-1.4 to -3.0	< -3.0
65	> -1.0	-1.0 to -2.6	< -2.6
70	> -0.8	-0.8 to -2.2	< -2.2
75	> -0.7	-0.7 to -2.1	< -2.1
80	> -0.6	-0.6 to -2.0	< -2.0
85	> -0.7	-0.7 to -2.2	< -2.2

5. Significance of Asymptomatic Bigeminy

What is the significance of asymptomatic bigeminy and other arrhythmias?

Submitted by: Anonymous

Specific treatment is required to prevent complications in some asymptomatic patients with arrhythmias such as atrial fibrillation (anticoagulation and rate control) and incessant atrial tachycardias (rate control to prevent tachycardia related heart failure).

Ventricular premature beats (VPBs) are of no prognostic significance in the absence of coronary artery disease (CAD), left ventricular (LV) systolic dysfunction or cardiomyopathy. The only treatment required is reassurance. If the patient has CAD or LV dysfunction, treatment should focus on risk factor reduction and optimizing β-blocker and ACE inhibitor. An implantable defibrillator may be indicated if LV ejection fraction is < 30% and there is no other significant comorbidity. Suppressing VPBs with antiarrhythmic drug therapy in patients with CAD actually causes more deaths.[1]

Look carefully at the electrocardiogram in a patient with VPBs. Is there any conduction abnormality, evidence of hypertrophy or infarction? If so, the patient should have an echocardiogram to detect structural abnormalities.

Premature atrial beats are benign and generally no investigations or treatment are required.

Reference
1. Echt DS, Liebson PR, Mitchell LB, et al: Mortality And Morbidity In Patients Receiving Encainide, Flecainide, Or Placebo. The Cardiac Arrhythmia Suppression Trial. N Engl J Med 1991; 324(12):781-8.

Answered by: Dr. Bibiana Cujec

6. Pediatric GERD

How long should a baby take lansoprazole for pediatric gastroesophageal reflux disease (GERD)?

Submitted by: Anonymous

Health Canada has not approved the use of lansoprazole or any PPI for babies under one-year-of-age. If this medication is prescribed to a baby (so called off-label use), then the baby should be followed by the prescribing physician to determine length of time of using this medication.

Answered by: Dr. Richmond Sy; and Dr. David Mack

7. Ankylosing Spondylitis

Can you have ankylosing spondylitis with negative x-rays?

Submitted by: Andre Lalonde, MD, Laval, Quebec

X-rays in ankylosing spondylitis are good tools to detect late stage disease when ankylosis, sclerosis and erosions have already occurred. However, plain x-rays are neither sensitive nor specific as diagnostic tools for early disease when the pathologic changes are not present.

If a diagnosis of ankylosing spondylitis is suspected, based on the clinical presentation of inflammatory back pain and the x-rays are reported as normal, then an MRI would be warranted. MRI is much more sensitive at detecting early disease changes such as marrow edema than x-ray, although it is not as specific as CT at detecting erosions. Given the availability of anti-TNF therapy and its effectiveness in treating ankylosing spondylitis, MRI can provide useful information to diagnose early disease.

When ordering an MRI for this problem, it is important to specify on the requisition that you are suspecting ankylosing spondylitis as the protocol is different than that for mechanical back problems. For inflammatory back pathology the ideal imaging is a short tau inversion recovery (STIR) weighted image in order to optimally visualize the degree of marrow edema.

Answered by: Dr. Michael Starr; and Dr. Sabrina Fallavollita

8. Investigating Frequent Watery Stools

How would you investigate a 42-year-old woman with a four month history of frequent watery stools, a negative travel history and generally feeling well?

Submitted by: Steven Goluboff, MD, Saskatoon, Saskatchewan

Investigation of this patient should begin with history and physical examination, with careful attention to medications (prescribed, OTC, herbal and antibiotics), family/personal history of autoimmune disease, celiac, Crohn's disease and ulcerative colitis. Dietary history looking for lactose intolerance and sorbitol ingestion is also important.

Laboratory investigations would include complete blood count, electrolytes, blood urea nitrogen, creatinine, liver enzymes, albumin, anti-tissue transglutaminase, IgA, TSH, inflammatory markers (C-reactive protein or erythrocyte sedimentation rate), iron studies (ferritin, iron, total iron-binding capacity), serum B12. Stools should be sent for culture and sensitivity, *C. difficile* toxin and ova and parasites.

Endoscopy would complete the work-up. Upper endoscopy with duodenal biopsies if celiac serology is positive. Colonoscopy with biopsies to look for inflammatory bowel disease or microscopic colitis.

Answered by: Dr. Robert Bailey and Dr. Karen I. Kroeker

9. Therapy Options for Smoking Cessation

What is the best therapy to help patients stop smoking?

Submitted by: Danaze Chambers, MD, Banff, Alberta

All patients should be assessed for smoking status, motivation to quit and motivators for and barriers to quitting. Motivation to quit can be classified as precontemplation (no plans to quit), contemplation (thinking about quitting but no plans) and preparations (plans to quit in near future). Common motivators to quit are health concerns, effects of smoking on others and social pressure. Common barriers to cessation are withdrawal, fear of failure and fear of weight gain. Many patients are precontemplators and thus the physician's role is often to use the patient's concerns as motivators for cessation and to suggest ways to decrease barriers to cessation. The advice to stop smoking should be done in a diplomatic and nonjudgmental approach. Firing or threatening to fire patients from medical practice because they could not or would not stop smoking is not helpful and may be considered unethical.

Although there are many therapies, there are no empirically-verified methods to match smokers to specific therapies. Most clinicians believe that patients should be informed of the various therapies and allowed to choose the therapy they believe will be most helpful. A combination of two or more of the following therapeutic approaches is recommended:

1. Behaviour therapy is the most widely accepted and well-proven psychological therapy for smoking
2. Nicotine replacement therapies double cessation rates, presumably because they reduce nicotine withdrawal. Replacement therapies use a short period of maintenance (six to 12 weeks) often followed by a gradual reduction period (six to 12 weeks). Nicotine gum is an OTC product that releases nicotine via chewing and buccal absorption. A 2 mg (for < 25 cigarettes/day smokers) and a 4 mg gum variety (for > 25 cigarettes/day smokers) are available. Smokers are to use one to two pieces of gum per hour after abrupt cessation. Adverse effects are minor and include bad taste and sore jaws. Nicotine patches, also sold OTC, are available in a 16-hour no-taper preparation and a 24- or 16-hour tapering preparation. Patches are administered each morning; compliance is high and the only major adverse effects are rashes and, with 24-hour wear, insomnia. Using gum and patches in high-risk situations increases quit rates by another 5% to 10%
3. Non-nicotine medication may be helpful to smokers who fail replacement therapy. Bupropion is an antidepressant medication that has both dopaminergic and adrenergic actions. Dosages of 300 mg q.d. reliably double quit rates in smokers with and without a history of depression. In one study, combined bupropion and nicotine patch had higher quit rates than either alone. Adverse effects include insomnia and nausea, but these are rarely significant. Seizures have not occurred in smoking trials

Answered by: Dr. Hany Bissada

10. Pseudoseizures

How does one treat pseudoseizures? Is there an evidence-based approach?

Submitted by: **Anne LaForte, MD,** Sarnia, Ontario

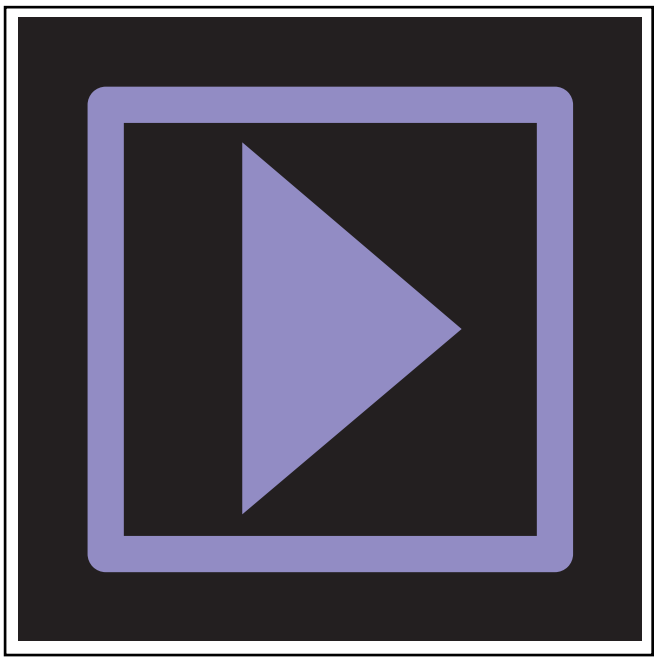
At this time, there is no evidence-based treatment for pseudoseizures, also called dissociative seizures, non-epileptic seizures and hysterical seizures. There have been only a few controlled studies looking at treatment for these events, generally with very few subjects, evaluating different types of psychotherapy. At present, in adults, cognitive behavioural therapy does seem to have some efficacy.

The major caveat is to make sure that you are actually treating pseudoseizures. Pseudoseizures are actually quite hard to diagnose and there is some controversy about how to do this. The "gold standard" for diagnosis, is that a patient has an unprovoked, typical event, while having video-electroencephalography (EEG) telemetry. The simultaneous EEG monitoring does not show any signs of epileptiform activity during the attack, if it is a true pseudoseizure. Pseudoseizures can frequently coexist with true epileptic seizures. In addition, other psychiatric disorders, such as panic disorder, can masquerade as pseudoseizures. If there is any question of the diagnosis, referral to a neuropsychiatrist or neurologist with experience in epilepsy and behavioural neurology is appropriate.

Resource

1. Goldstein LH, Deale AC, Mitchell-O'Malley SJ, et al: An Evaluation of Cognitive Behavioral Therapy as a Treatment for Dissociative Seizures: A Pilot Study. Cogn Behav Neurol 2004; 17(1):41-9.

Answered by: **Dr. Inge Loy-English**



11. Ruptured Tympanic Membrane

What is the treatment for a ruptured tympanic membrane?

Submitted by: Randi Morris, MD, Montreal, Quebec

A tympanic membrane (ear drum) can be ruptured as a result of multiple etiologies. Firstly, it can be as a result of infection (this commonly occurs in children). An acute otitis media can rupture the tympanic membrane, allowing escape of the turbid middle ear fluid. This often results in an improvement in symptoms including otalgia. Rupture secondary to trauma can result from either a very loud noise (explosion) or mechanical trauma to the external ear. Finally, iatrogenic causes can include a persistent perforation occurring after a myringotomy and tube placement. The majority of these heal spontaneously when the ventilation or t-tube falls out. However, a small proportion remains, as a long-term perforation.

The vast majority of perforations heal spontaneously. Occasionally, perforations require surgical intervention to close them. This is called a myringoplasty and involves a general anesthetic. Very small perforations are repaired by freshening the perforation edges and performing an "onlay" graft (*e.g.*, fat, fascia). Larger perforations are repaired with an underlay myringoplasty. In this case, the tympanic membrane is elevated and an underlay graft placed beneath the perforation. The tympanic membrane is then re-positioned. It is successful in approximately 85% of cases. If it fails, it is often as a result of infection.

Answered by: Dr. Jonathan Irish; Dr. Sanjay Verma; and Dr. Emma Barker

12. Testosterone Testing

Since testosterone testing is so inaccurate as a reflection of deficiency, can a patient with symptoms be given a trial of testosterone?

Submitted by: John D. Shier, MD, Ottawa, Ontario

In my opinion, this should not be done. Testosterone testing should be done in the morning when levels are generally higher. If available, a free testosterone should be done or by measuring sex hormone binding globulin levels, free testosterone can be estimated. Other testing that can be performed for further evaluation include luteinizing hormone, follicle stimulating hormone and prolactin levels.

Answered by: Dr. Vincent Woo

13. Combining Yasmin and Spironolactone to Treat Acne

Can Yasmin and spironolactone be combined for acne treatment or if Yasmin does not work, does spironolactone not work?

Submitted by: Theo Kemp, MD, Blackfalds, Alberta

Yasmin is an OC containing 30 ug of ethinyl estradiol and 3 mg of drospirenone. Drospirenone is a non-androgenic and non-estrogenic steroid derived from 17 α-spironolactone and has both anti-aldosterone and anti-androgenic properties. Yasmin is particularly useful when an OC is needed in a woman with an androgen induced condition such as acne vulgaris. As well, if a woman is sexually active and of childbearing potential, birth control such as an OC is necessary because of the risk of feminization of a male fetus if she were to become pregnant while taking an anti-androgen. Spironolactone can be used alone as an anti-androgen for acne but it is often combined with an OC to ensure pregnancy does not occur.

Combining Yasmin and oral spironolactone makes sense, as this combination would increase the anti-androgen effect and should be an effective treatment for acne vulgaris. However, the concern is whether this combination would increase side-effects, especially the risk of hyperkalemia.

I am aware of only one article where Yasmin and oral spironolactone were combined to treat 27 women with severe acne who had failed one previous standard acne treatment including eight patients in whom acne recurred after isotretinoin therapy.

Spironolactone was given in a dose of 100 mg q.d. All subjects tolerated the combination of the two medications and none had to discontinue either of the medications. No significant elevation of potassium was found in any of the subjects.

At follow-up, 85% of subjects had excellent improvement or complete clearing of their acne lesions.

Based on this small study, it would appear to be safe to combine Yasmin with spironolactone (in doses of 100 mg q.d.) but the authors recommended the results be confirmed with a larger series of patients.

Resource
1. Krunic A, Ciurea A, Scheman A: Efficacy And Tolerance Of Acne Treatment Using Both Spironolactone And A Combined Contraceptive Containing Drospirenone. J Am Acad Dermatol 2008; 58(1):60-2.

Answered by: Dr. Richard Haber

Yasmin is particularly useful when an OC is needed in a woman with an androgen induced condition such as acne vulgaris.

14. A Pregnant Woman Suffering From Pruritus

Can you suggest treatment for a pregnant woman in the third trimester suffering from pruritus as a result of cholestasis and cholestyramine is not effective?

Submitted by: Adam Kayumi, MD, Mississauga, Ontario

Additional therapies for pruritus associated with cholestasis of pregnancy include antihistamines, calamine or chamomile lotions, topical corticosteroids, loose clothing and the avoidance of hot or humid temperatures. Dexamethasone, which is used to induce lung maturity prior to 34 weeks gestation, may be considered. Once term is achieved and depending on the severity of the symptoms, induction can be offered. Of note, the liver is responsible for the clearance of fetal waste so close monitoring of maternal liver functions and fetal well-being is suggested to reduce the risk of fetal complications. If cholestyramine, which has limited efficacy, is used the newborn may have lower levels of vitamin K due to reduced absorption from the GI tract.

Answered by: Dr. Victoria Davis

See prescribing summary on page 106

15. Cross-Reactivity Between Fruits and Nuts

Please comment on the cross-reactivity between fruits and nuts.

Submitted by: Lucie Dessureault, MD, Shawinigan-Sud, Quebec

Thus far, two notable cross-reactivities include mango with pistachio/cashew, as well as hazelnut as part of the pollen-food allergy syndrome.

Mango, together with pistachio and cashew, belongs to the Anacardiaceae family. All three foods may cause severe anaphylactic reactions. Cross-reactivity has been found among pistachio nut, cashew nut and mango seed, but this cross-reactivity did not extend to mango pulp. It is possible that pistachio and cashew nut-sensitive patients may tolerate mango since only the pulp is usually consumed. However, more studies are needed to completely understand the cross-reactivity between mango fruit and nuts of this family. Most mango associated reactions reflect oral symptoms as part of the oral allergy syndrome and cross-reactivities among mango fruit allergens and mugwort pollen (a weed), birch pollen, celery, carrot and apple have been described. Mango allergen can be quite stable during technical processing, resulting in preservation of allergenicity and thus increasing the potential for systemic reactions in allergic individuals.

The oral allergy syndrome has more recently been renamed pollen-food allergy syndrome. In this condition, hayfever patients sensitized to pollen develop oral allergic symptoms to certain fruits and vegetables. The birch pollen-apple oral allergy syndrome is the most common. The major birch pollen pan-allergen Bet v 1 has a very similar structure to the major allergens in apple, as well as hazelnut and some other vegetables (carrot, cherry, pear, tomato, celery, potato and peach). Allergy to any combinations of these is possible. Although the typical forms of this entity do not require epinephrine precautions, some of these patients have been known to progress to more serious upper airway reactions. An assessment by an allergist to delineate these relationships and assess potential severity is important. In the case of any nut allergy, I would ensure that the patient carries an epinephrine autoinjector.

Resource

1. Fernández C, Fiandor A, Martinez-Garate A, et al: Allergy To Pistachio: Crossreactivity Between Pistachio Nut And Other Anacardiaceae. Clin Exp Allergy. 1995; 25(12):1254-9.

Answered by: Dr. Tom Gerstner

16. How to Treat Relapsing *C. Difficile*

How to treat relapsing *C. difficile* infection?

Submitted by: Craig Render, MD, Kelowna, British Columbia

The treatment of *C. difficile* infection may be difficult. The first step in management of *C. difficile* diarrhea is to stop the precipitating antibiotic and conservative therapy with fluid and electrolyte management. The initial antibiotic of choice is metronidazole but relapse rate after therapy is up to 30%. Vancomycin is the accepted second-line antibiotic to treat *C. difficile*. The dose is usually 125 mg q.i.d. to 500 mg q.i.d. for 10 to 14 days. Relapsing *C. difficile* infection is often difficult to treat and multiple episodes are not uncommon. There are numerous approaches to relapsing infection. A repeat course of metronidazole or vancomycin for another 14 days is reasonable. This strategy may be successful in about 40% of cases of difficult to treat *C. difficile*. A prolonged or pulsed antibiotic therapy has been studied—vancomycin for three weeks followed by a taper to every other day for one week and every third day for a final week. This approach is based on the theory that recurrence is caused by spores that are resistant to antibiotics and then convert to toxin producing bacteria after the antibiotics are discontinued. Binding resins such as cholestyramine to bind toxins have been evaluated. The use of probiotics to restore the normal colonic flora have gained popularity though controlled trials are lacking. Other approaches such as fecal enemas have also been tried to restore normal colonic flora.

Resource
1. Feldman M, Friedman LS, Brandt LJ: *Sleisenger and Fordtran's Gastrointestinal and Liver Disease*. Eighth Edition. Saunders, 2006. p.2402-2407.

Answered by: Dr. Richmond Sy

17. Levothyroxine and Iron Supplements

Considering there is an interaction between levothyroxine and iron supplements, how do you advise a patient who has hypothyroidism and is on levothyroxine, but requires iron for anemia?

Submitted by: Soheir Atalla, MD, Montreal, Quebec

It is recommended that levothyroxine be taken on an empty stomach for optimal absorption. If medications such as iron supplements are needed, they should be taken at other times of the day separate from other medications.

Answered by: Dr. Vincent Woo

18. Adult Onset ADHD

What are the newest treatments (medications) for adult onset ADHD?

Submitted by: Brad Atkinson, MD, Sheet Harbour, Nova Scotia

Pharmacotherapy remains the cornerstone of treatment for adult attention-deficit/hyperactivity disorder (ADHD). In general, current conclusions are that the drugs useful for ADHD in children are useful in the management of adults with the disorder. Medications used in ADHD are divided into stimulant medications and non-stimulant medications.

Stimulant medications are the most frequently prescribed. They include methylphenidate preparations and amphetamine preparations.

Non-stimulant medications include atomoxetine and bupropion.

Atomoxetine is a non-stimulant medication approved for the treatment of ADHD in both children and adults. It is a selective norepinephrine reuptake inhibitor and does not appear to affect the dopamine systems as directly as do the stimulants. It is often prescribed once per day, initially 40 mg q.d. and if well tolerated, the dose can be increased to 80 mg q.d. Common side-effects are headache, abdominal pain, nausea, vomiting, weight loss, anxiety, sleepiness and insomnia. It can also interfere with sexual performance in adults.

Bupropion SR and XL have been used to treat ADHD for several years. A recent controlled study showed that it is effective in the treatment of ADHD symptoms in adults. Its structure is chemically similar to amphetamine, but does not have the same abuse potential. It should not be used in individuals with bulimia or a seizure disorder. It is useful for individuals who cannot tolerate stimulants or for whom a Schedule II drug is inadvisable.

Although they are less effective than stimulant medications, non-stimulant medications have particular usefulness in patients in whom stimulants are contraindicated (*e.g.*, those patients with substance abuse).

Answered by: Dr. Hany Bissada

19. C-Reactive Protein in Patients with Acute Coronary Syndrome

Should all patients with acute coronary syndrome have a C-reactive protein (CRP) measured?

Submitted by: Mohamed Ravalia, MD, Twillingate, Newfoundland

There is no evidence to routinely measure levels of CRP in patients with acute coronary syndrome (ACS). CRP is a marker of inflammation, which is one of the mechanisms by which atherosclerosis progresses to plaque rupture and ACS. Elevated levels of CRP (at admission) do suggest increased risk of adverse outcome. One month after an ACS, patients with elevated CRP also have increased risk. Despite the fact that "anti-inflammation" therapies (*i.e.*, statins) are used as secondary prevention after an ACS, the use of CRP has not been specifically evaluated as a marker to monitor therapy post-ACS.

Answered by: Dr. Richard Sheppard

20. Teenage Male Pattern Baldness

Is any treatment effective and safe for young men (late teens, early 20's) with male pattern baldness?

Submitted by: John McCleave, MD, Rexton, New Brunswick

Male pattern hair loss, also known as androgenetic alopecia, is a non-scarring alopecia so common it is considered a secondary sexual characteristic. By age 70, nearly 80% of men experience this type of alopecia. Although more common in the mid to late 20's, some young men in their teens and early 20's are also affected.

Affected males have hair follicles that are particularly sensitive to dihydrotestosterone (DHT)—testosterone is converted to DHT in certain tissues including the scalp by type II 5-α-reductase.

Early treatment can prevent further hair loss, may encourage regrowth and improve patients' quality of life.

Minoxidil was initially developed to treat hypertension as a potent vasodilator. It was subsequently found to promote hair growth. Topical minoxidil (2% and 5% solutions) is applied (approximately 1 ml) twice daily indefinitely, as stopping or reducing the dose allows for continued alopecia. One-third of patients may have good regrowth. It is thought to stimulate follicular vascularity and proliferation. There is minimal systemic absorption and has been used safely in large trials.[1] Drawbacks include local irritation and hypertrichosis if it inadvertently contacts areas not on the scalp.

Oral finasteride (1 mg q.d.) is an option for patients > 18-years-old and may be more effective than topical minoxidil.[2] It inhibits type II 5-α-reductase, thus decreasing scalp and serum levels of DHT. The main concern in males is sexual dysfunction. Nearly half of patients will note improved appearance of their hair.[3]

If these are not effective, or if patients are interested, a variety of surgical options exist (*e.g.*, hair transplantation).

References
1. Shapiro J: Safety Of Topical Minoxidil Solution: A One-Year, Prospective, Observational Study. J Cutan Med Surg 2003; 7(4):322-9.
2. Arca E, Açikgöz G, Taştan HB, et al: An Open, Randomized, Comparative Study Of Oral Finasteride And 5% Topical Minoxidil In Male Androgenetic Alopecia. Dermatology 2004; 209(2):117-25.
3. Leyden J, Dunlap F, Miller B, et al: Finasteride In The Treatment Of Men With Frontal Male Pattern Hair Loss. J Am Acad Dermatol 1999; 40(6 Pt 1):930-7.

Answered by: Dr. John Kraft; and Dr. Charles Lynde

21. Screening for Bone Loss

Should we screen routinely for bone loss in young patients who are on long-term anticonvulsant medication?

Submitted by: Ruth Adler, MD, Kitchener, Ontario

There is increasing evidence that exposure to anti-epileptic drugs (AEDs) is a risk factor for the development of osteoporosis. In ambulatory patients, long-term antiepileptic therapy has been associated with low bone density in cross-sectional as well as in prospective studies. Decrease in BMD was seen as early as six months after initiating these medications.

Decreased circulating levels of vitamin D may occur in patients on chronic anticonvulsant medications, due to induction of P450 enzyme activity, which can in turn inactivate vitamin D metabolites.

Recently, the National Osteoporosis Foundation (NOF) recommended screening for adults taking medications associated with low bone mass or bone loss which would include chronic anticonvulsant therapy. It may be reasonable, in light of the more recent data, to obtain a baseline BMD in these patients since one would expect that there may be progressive bone loss over time and that these patients will require ongoing monitoring. In addition, all patients should be counselled on the importance of exercise and adequate intake of calcium (1500 mg q.d.) and vitamin D (800 IU q.d.).

Answered by: Dr. Michael Starr; and Dr. Ahmad Al-Enizi

22. Reliability of Cervical Length Assessment

How reliable is cervical length assessment in the prediction of preterm labour?

Submitted by: Maureen Conly, MD, North Vancouver, British Columbia

In a review of transvaginal ultrasonographic cervical length measurement in predicting preterm birth in asymptomatic women considered at increased risk (because of a history of spontaneous preterm birth, uterine anomalies or excisional cervical procedures), cervical length measured by transvaginal ultrasonography predicted spontaneous preterm birth. The shorter the cervical length cut-off, the higher the positive likelihood ratio (LR). The most common cervical length cut-off was < 25 mm. Using this cut-off to predict spontaneous preterm birth < 20 weeks gestation revealed LR+ = 4.31 (95% CI, 3.08-6.01); at 20 to 24 weeks, LR+ = 2.78 (95% CI, 2.22-3.49); and at > 24 weeks, LR+ = 4.01 (95% CI, 2.53-6.34). In women with a history of spontaneous preterm birth cervical length at < 20 weeks revealed LR+ = 11.30 (95% CI, 3.59-35.57) and at 20 to 24 weeks LR+ = 2.86 (95% CI, 2.12-3.87), but there were limited data on > 24 weeks. Cervical length measured by transvaginal ultrasonography in asymptomatic high-risk women predicts spontaneous preterm birth at < 35 weeks.

Resource

1. Crane JM, Hutchens D: Transvaginal Sonographic Measurement Of Cervical Length To Predict Preterm Birth In Asymptomatic Women At Increased Risk: A Systematic Review. Ultrasound Obstet Gynecol 2008; 31(5):579-87.

Answered by: Dr. Victoria Davis

23. Wegener's Granulomatosis

Is there a genetic basis for Wegener's granulomatosis?

Submitted by: Gordon Young, MD, Pictou, Nova Scotia

Dr. Friedrich Wegener described this condition in 1936. It is a form of vasculitis that can affect many organs in the body, including those in the head and neck. It is associated with abnormal circulating antibodies against neutrophils, known as anti-neutrophil cytoplasmic antibodies (ANCA). These antibodies are thought to be responsible for the inflammatory process seen in Wegener's granulomatosis. These antibodies react with proteinase 3, an enzyme within the neutrophil granulocyte (within the cytoplasm) and are known as cANCA (cytoplasmic, in contrast with the pANCA, perinuclear). Raised cANCA can help with the diagnosis, but raised levels are not conclusive and low levels do not allow rejection of the diagnosis.

The exact cause for the production of ANCAs is unknown, although some drugs have been implicated in secondary forms of Wegener's. As with many autoimmune disorders, there may be some form of genetic predisposition combined with molecular mimicry caused by a virus or bacterium. However, compared with diseases that have obvious genetic predisposition, genetic causes appear to play a relatively small role in Wegener's. It is very unusual for Wegener's to occur in two people in the same family.

Diagnosis is often severely delayed due to the non-specific nature of the symptoms. Interestingly, rhinitis is often one of the first signs in most patients. Later, signs in the nose include nosebleeds, septal perforation and a saddle nose deformity.

Treatment depends on the severity of the condition. Medical management includes a combination of steroids, immunosuppressive agents and antibiotics. Prior to the 1970's this condition was usually fatal within 12 months. However, the advent of cyclophosphamide in the treatment of this condition significantly altered the disease outcome.

Answered by: Dr. Jonathan Irish; Dr. Sanjay Verma; and Dr. Emma Barker

24. Vascular Depression

What is your opinion about vascular depression and if it exists, how can we make the diagnosis?

Submitted by: Raouf Dimitry, MD, Edmonton, Alberta

Depression is common after stroke and myocardial infarction (MI) and increases mortality and morbidity. Whether cerebral atherosclerotic disease without acute vascular events results in depression is still debated. The vascular depression hypothesis was put forward by Alexopoulos and his group from Cornell University in 1997.[1] They postulated that cerebrovascular disease may predispose, precipitate or perpetuate depression in the geriatric population. Depression, vascular disease, vascular risk factors and ischemic brain lesions (particularly in the left prefrontal cortex) often coexist in the elderly and it is difficult to ascertain whether depression is a result of these brain lesions or just an association of two common conditions.

Patients with vascular depression often have poorer outcomes and this may be related to a higher prevalence of executive dysfunction and consequent disability. Depressed patients with vascular risk factors are also at higher risk for developing vascular dementia.

Characteristics of vascular depression include:

1. Late onset depression
2. Vascular risk factors: diabetes, hypertension, hypercholesterolemia, smoking history or evidence of vascular disease including peripheral arterial disease, prior MI, stroke
3. Ischemic changes on brain imaging studies
4. Greater psychomotor retardation, anhedonia and apathy rather than sadness, less agitation, less guilt, more cognitive impairment especially frontal executive impairment manifested by difficulties with motivation, organization, planning, sequencing and abstracting, worse functional impairment, less insight and lower incidence of psychosis

Preliminary data suggest that these patients may preferentially respond to non-standard antidepressant therapy, including older antidepressants, combination therapies, or electroconvulsive therapy.

Reference

1. Alexopoulos GS, Meyers BS, Young RC, et al: 'Vascular Depression' Hypothesis. Arch Gen Psychiatry 1997; 54(10):915-22.

Answered by: Dr. Bibiana Cujec

25. Multiple Seborrheic Keratoses

Is there any help for patients with multiple seborrheic keratoses? Is imiquimod being used off-label for this?

Submitted by: Stephanie Popiel, MD, Perth, Ontario

There are no evidence-based effective topical treatments for seborrheic keratoses. Liquid nitrogen cryotherapy remains the treatment of choice. Surgical treatment with curettage and electrodesiccation, surgical excision and laser can be effective but are much more likely to leave scars.

Imiquimod 5% cream is an immune stimulator and would not be expected to help in the treatment of seborrheic keratoses. In one open study in which it was tried as an off-labelled treatment for seborrheic keratoses, imiquimod was ineffective when used once daily and twice a day. This open study did find some clinical and histological response to treatment with topical tazarotene 0.1% cream used twice a day but no effect when used once daily.

Other topical agents that have been reported to give some clinical response in height reduction of seborrheic keratoses in open studies include 12% ammonium lactate lotion and a combination of 5% benzoyl peroxide daily in combination with topical terbinafine (acting as a tertiary amine). Neither of these treatments gave good clinical results.

Because of the lack of evidence-based studies that topical agents are helpful in treating seborrheic keratoses and limited open studies demonstrating significant clinical improvement, topical agents should be avoided in the treatment of seborrheic keratoses.

Resource
1. Herron MD, Bowen AR, Krueger GG: Seborrheic Keratoses: A Study Comparing The Standard Cryosurgery With Topical Calcipotriene, Topical Tazarotene And Topical Imiquimod. Int J Dermatol 2004; 43(4):300-2.

Answered by: Dr. Richard Haber

26. Contracting *H. Pylori*

How does one get *H. Pylori*?

Submitted by: Jean-Robert Timothee, MD, Greenfield Park, Quebec

Transmission of *H. pylori* is person to person. Humans are the primary reservoir of *H. pylori*, though it has also been found in the stomachs of cats and sheep. The possible methods of transmission include fecal-oral, oral-oral and gastro-oral. Several studies demonstrate a higher incidence of *H. pylori* infections among family members where there is an infected parent or child.

Resource
1. Feldman M, Friedman LS, Brandt LJ: *Sleisenger and Fordtan's Gastrointestinal and Liver Disease*. Eighth Edition. Saunders, 2006. p.1050-1051.

Answered by: Dr. Richmond Sy

27. Guidelines for Routine Cardiac Testing

Please outline guidelines for routine cardiac testing for men and women.

Submitted by: Carrie Beallor, MD, Thornhill, Ontario

The optimal predictive accuracy of cardiac testing requires careful patient selection as well as state-of-the-art equipment, technical expertise in data acquisition and the availability of an experienced and adequately trained physician for interpretation. Most cardiac tests have lower specificity (a high false positive rate) when performed in patients with a low pretest likelihood of CVD. The clinical uncertainty and patient anxiety that follows often results in the need for additional and sometimes more invasive testing to clarify the results and reassure everyone concerned (patient, family, referring physician, employer, insurance company, *etc.*).

The INTERHEART study suggested that up to 90% of heart attacks and strokes can be predicted by physicians through a careful patient history, BP assessment and fasting glucose and lipid profile measurement. Cardiac testing should therefore never be "routine" but should be reserved for patients with symptoms suggestive of CVD or those who are at intermediate to high global CVD risk based on basic clinical evaluation and blood testing. When referring a patient for cardiac testing, physicians should take note of the tremendous variability in the quality of cardiac tests provided in Canada at present due to the lack of infrastructure to ensure a minimal standard of performance and quality control. Physicians and patients are strongly urged to select a cardiac testing center on the basis of the quality and reliability of the report provided rather than the length of the waiting list for an appointment.

Answered by: Dr. George N. Honos

28. Quetiapine in Thyroid Disease

Is quetiapine contraindicated in thyroid disease?

Submitted by: Cathy Cameron, MD, Toronto, Ontario

Quetiapine and other second generation antipsychotics are not contraindicated for individuals with thyroid disease. There are reports of some mild alterations in levels but these changes in thyroid function tests are usually not clinically significant.

Answered by: Dr. Vincent Woo

29. Treatment for Scabies

Please provide a surefire treatment/remedy for scabies.

Submitted by: Peter T. C. Lee, MD, New Glasgow, Nova Scotia

Human scabies is caused by the highly host-specific mite, *Sarcoptes scabiei*. It produces an intensely pruritic skin condition. Scabies treatment involves topical scabicides. Permethrin 5% is the preferred topical scabicide due to its low toxicity and excellent results. It is effective during all stages of the life cycle of the parasite. Adverse events are rare; however, there may be mild stinging on application. The cream should be applied from the neck down and washed off after eight to 12 hours. The patient should pay particular attention to warm, moist areas preferred by the mite, such as the intergluteal cleft, digit creases, skin under nails and umbilicus. In adults, the scalp may be excluded from treatment, whereas in infants studies have shown a prevalence of scabies on the scalp as high as 41%. No cases of true resistance have been documented. Permethrin 5% is not recommended during pregnancy and for infants younger than two-months-of-age. Permethrin 5% should not be confused with the 1% permethrin solutions that are effective for treating head lice but not scabies.

To reduce the potential of reinfestation by fomite transmission, linens, clothing and towels used in the past week by the patient should be washed in hot water and dried on high heat. Since asymptomatic carriers are common, all individuals in the same household or who are in close personal contact with the affected patient should be treated simultaneously, even in the absence of clinical symptoms, to prevent reinfestation. An explanatory leaflet often helps with adherence.

Patients should be advised that lesions and pruritus may persist for two to four weeks after treatment ("post-scabetic pruritus"). It occurs due to the body's immune reaction to remnants of the killed mites and does not necessarily imply treatment failure. An oral antihistamine or topical corticosteroid may be used to control the itching.

Most patients experience relief from pruritus three days after treatment. A second course of treatment is usually repeated seven days after the initial round to kill any hatchlings that survived the initial treatment and are about to reach the reproductive stage.

Ivermectin is not yet licensed in North America as an oral treatment for scabies. This oral antiparasitic agent successfully cures scabies after one dose and is repeated in a week's time. It has been successfully used when other scabicide treatments have failed, especially for patients with Norwegian scabies. Ivermectin blocks γ-aminobutyric acid and glutamate neurotransmission in mites but does not cross the blood brain barrier or placenta so it is not toxic to humans. Dx

Answered by: Dr. John Kraft; and Dr. Charles Lynde