Experts on Call

Answers to your questions from our medical experts

1. Diagnostic Criteria for Hypertension

Is there any evidence that our present diagnostic criteria for hypertension are too high?

Submitted by: M. Krieger, MD, Toronto, Ontario

Current diagnosis of hypertension is made based on office blood pressures of > 140/90 mmHg in nondiabetic individuals and > 135/85 mmHg in patients with diabetes. There is a linear relationship between an increase in blood pressure and cardiovascular events from a systolic pressure of more than 115 mmHg. A recent meta-analysis of antihypertensive treatment for secondary prevention of CV events in patients without hypertension found that antihypertensive therapy was associated with decreased risk of stroke, heart failure, and all-cause mortality.[1] Most of the trials in the meta-analysis involved the use of ACE inhibitors and ARBs in patients with myocardial infarction, so it can not be concluded that blood pressure lowering was the only mechanism of benefit of the antihypertensive therapy.

A reasonable approach is to advocate lifestyle changes in patients with prehypertension (BP systolic 129 to 139 mmHg and diastolic pressures 80 to 89 mmHg). Patients should be counseled to lose weight, exercise, and decrease their alcohol intake. It is premature to advocate drug therapy in patients with blood pressures < 140/90 mmHg.

Reference
1. Thompson AM, Hu T, Eshelbrenner CL, *et al*: Antihypertensive Treatment and Secondary Prevention of Cardiovascular Disease Events Among Persons with Hypertension: A Meta-analysis. JAMA 2011; 305(9):913–922.

Answered by: Dr. Bibiana Cujec

2. Target LDL

What is the target LDL for patients with impaired glucose tolerance?

Submitted by: Vona MacMillan, MD, Dalhousie, New Brunswick

There is no strong data for this population (unlike patients with overt diabetes mellitus), although they are at higher risk for vascular disease. It is best to use one of the risk engines to calculate CV risk and determine target LDL based on that. Some risk engines that have been validated include Framingham and Reynolds.

Answered by: Dr. Ally Prebtani

3. Treatments for Chronic Insomnia

? Many of my patients suffer from chronic insomnia, and I am leery of prescribing sleeping medication, which may be addictive and also contribute to dementia development. What should be done medically and nonmedically?

Submitted by: **Paul Stephan, MD,** Scarborough, Ontario

Treatment of insomnia depends upon the underlying cause. If an underlying medical or sleep disorder is suspected, it should be ruled out first. Behaviour changes, learned through cognitive behavioural therapy, may provide significant help to chronic insomnia patients. The principles of sleep hygiene, which are given below, should also be followed:

- Regulating the sleep wake cycle
- Regulating the amount of sleep obtained each night
- Exercising daily and regularly but not in the late evening
- Doing something relaxing before bedtime
- Keeping a fixed bedtime and wake time even on weekends
- Increasing daytime physical activity
- Limiting daytime naps to less than an hour
- Avoiding caffeine and nicotine in the evening
- Avoiding sleep when hungry or with a full meal; however, one may have a light snack
- Avoiding fluids in late evening
- Using a soft pillow and a firm mattress
- Avoiding hot showers in the evening; one may take a lukewarm bath
- Making sure the bedroom is quiet with a comfortable temperature
- If one still can't fall sleep, getting out of bed and reading for 15 to 20 minutes, then trying to sleep, may be useful

If these strategies are not helpful and medications are required, sleeping medications may be prescribed only for two to four weeks to reduce the risk of dependency. However, sometimes a particular medication may not be helpful and may need to be replaced with another. Medications, such as zolpidem 5 to 10 mg or short-acting benzodiazepines, such as triazolam 0.125 to 0.5 mg h.s., which has a half-life of only two to three hours, are considered to be safe.[1]

Reference
1. Sullivan SS: Insomnia Pharmacology. Medical Clin North Am 2010; 94(3):563–580.

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

4. Blood Tests to Diagnose Celiac Disease

What blood tests can be done to diagnose Celiac disease?

Submitted by: M. Krieger, MD, Toronto, Ontario

There are several blood tests that can be used to diagnose Celiac disease. The first widespread serologic tests were the antigliadin antibodies (IgA and IgG). They had a specificity of 78 to 86% and a sensitivity of 52 to 86%. They are enzyme-linked immunosorbent assays. Nowadays, they have been replaced by IgA antiendomysial antibody (EMA) and IgA tissue transglutaminase antibody (tTGA) tests.

EMA is an indirect immunofluorescence assay, which is more specific (> 95%) and sensitive (> 90%) than gliadin-based tests, but it is qualitative, more time consuming, and more operator dependent than tTGA. Many studies show tTGA specificity to be greater than 95% and sensitivity to be in the range of 90 to 96%.

Therefore, tTGA is the single best serologic test for Celiac disease. The addition of other serologic tests does not seem to confer any additional utility in diagnosing Celiac disease.

Nonserologic tests, such as HLA-DQ2 and HLA-DQ8, are also available. Almost all patients with Celiac disease have either DQ2 (95%) or DQ8 (5%) alleles, but approximately 40% of the population can also have HLA positive testing. Therefore, testing HLA provides almost 100% negative predictive value, and it may be a useful add-on to serologic based tests.

Resource

1. AGA Institute: AGA Institute Medical Position Statement on the Diagnosis and Management of Celiac Disease. Gastroenterology 2006; 131(6):1977–1980.

Answered by: Dr. Richmond Sy

5. Selecting a Pneumococcal Vaccine

What is the difference between the three pneumococcal vaccines? Which age group gets which one?

Submitted by: Ingrid Maria Jarvis, MD, Toronto, Ontario

Two vaccine types are available for the prevention of invasive pneumococcal infections: conjugate and polysaccharide vaccines. Two conjugate vaccines (Prevnar®13 [13-valent] and Synflorix® [10-valent]) and two polysaccharide vaccines (Pneumovax®23 [23-valent] and Pneumo®23 [23-valent]) are approved for use in Canada.[1,2]

The long-term efficacy of the conjugate pneumococcal vaccines is unknown, but immunologic memory has been demonstrated to last for 18 to 20 months in young children.[1]

In healthy young adults, a single dose of polysaccharide vaccine produces type-specific protection of > 80%.[1] The degree of protection declines to 50% to 80% in the elderly and with certain comorbidities (*e.g.*, diabetes mellitus, asplenia).[1] In general, children under two respond poorly to polysaccharide vaccine, and it is therefore not recommended for this age group.[1] Following polysaccharide pneumococcal immunization, serotype-specific antibody levels decline after 5 to 10 years; they decrease more rapidly in some groups than others.[1] The duration of immunity is unknown.

The National Advisory Committee on Immunization (NACI) currently recommends Prevnar®13 as the vaccine of choice for the routine immunization of infants and children.[2] Dosing schedules vary across the country. NACI also recommends a single dose of conjugate vaccine for children over 60-months-old who are at risk of invasive disease (*e.g.*, asplenia, cirrhosis, chronic renal failure or nephritic syndrome, and HIV infection). Conjugate pneumococcal vaccine is not yet routinely recommended for adults.

Pneumococcal polysaccharide vaccine is approved for use in those over two-years-old who are at risk for invasive pneumococcal disease as well as for all persons over 65-years-old. Some experts recommend that for unimmunized persons who are over two-years-old, the conjugate vaccine should be given as the initial dose, followed by the polysaccharide vaccine, as this may theoretically improve antibody response and immunologic memory.[1] However, if only one vaccine can be provided, it should be the polysaccharide vaccine.

References
1. Pneumococcal Vaccine. Canadian Immunization Guide, 2006. http://www.phac-aspc.gc.ca/publicat/cig-gci/p04-pneu-eng.php#approve. Accessed: September 5, 2012.
2. National Advisory Committee on Immunization. (2010). Update on the Use of Conjugate Pneumococcal Vaccines in Childhood. Canadian Communicable Disease Report, 36 (ACS-12). http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/10vol36/acs-12/index-eng.php. Accessed: September 6, 2012.

Answered by: Dr. Ameeta Singh
Ms. Anita Hanrahan

6. Preventative Bisphosphonate Therapy for Breast Cancer

Is it reasonable to treat a woman at high-risk for breast cancer with preventative bisphosphonate therapy?

Submitted by: Kyra Simmons, MD, Calgary, Alberta

In breast cancer prevention trials, women at increased risk for breast cancer include those who:

- Are over 35-years-of-age with a history of ductal carcinoma in situ (DCIS), lobular carcinoma in situ (LCIS), or atypical ductal or lobular hyperplasia (ADH/ALH)
- Are between the ages of 35- and 59-years-of-age with a Gail model risk of ≥ 1.66% over five years
- Are over 60
- Have BRCA1 or BRCA2 mutations without prophylactic mastectomy

Currently, the use of bisphosphonates in the primary prevention of breast cancer can not be recommended, as prospective clinical trial data is lacking. Observational studies have reported associations between oral bisphosphonate use and decreased breast cancer incidence.[1–3] In patients at high-risk for breast cancer, the selective estrogen-receptor modulators (SERMs) tamoxifen and raloxifene (the latter in postmenopausal women only) may be considered after a discussion of the risks and benefits.[4] Recent evidence from a prospective, phase III clinical trial in postmenopausal women has also shown that the aromatase inhibitor exemestane reduces the incidence of estrogen-receptor (ER) positive invasive breast cancer compared to placebo, although long-term follow-up is not yet mature.[5]

References
1. Rennert G, Pinchev M, Rennert HS: Use of Bisphosphonates and Risk of Postmenopausal Breast Cancer. J Clin Oncol 2010; 28(22): 3577–3581.
2. Chlebowski RT, Chen Z, Cauley JA, *et al*: Oral Bisphosphonate Use and Breast Cancer Incidence in Postmenopausal Women. J Clin Oncol 2010; 28(22):3582–3590.
3. Newcomb PA, Trentham-Dietz A, Hampton JM: Bisphosphonates for Osteoporosis Treatment Are Associated with Reduced Breast Cancer Risk. Br J Cancer 2010;102(5):799–802.
4. Nelson HD, Fu R, Griffin JC, *et al*: Systematic Review: Comparative Effectiveness of Medications to Reduce Risk for Primary Breast Cancer. Ann Intern Med 2009; 151(10):703–715.
5. Goss PE, Ingle JN, Alés-Martínez JE, *et al*: Exemestane for Breast-cancer Prevention in Postmenopausal Women. N Engl J Med 2011; 364(25): 2381–2391.

Answered by: Dr. Roger Y. Tsang

7. Detection and Management of Placenta Previa

Placenta previa — how can the diagnosis be made as early as possible, and what measures can be taken to reduce the risk of bleeding?

Submitted by: Mark D'Souza, MD, Winnipeg, Manitoba

The suspicion of a placenta previa is usually found during the 18 to 20 week gestation ultrasound. However, the relationship of the placenta and the lower uterine segment changes with advancing gestation as the lower uterine segment begins to thin and expand. In addition, a transabdominal ultrasound is less accurate than a transvaginal ultrasound, as the vertex, obesity, and bladder volume play a role in visualization of the placenta and its relationship to the internal os, especially if the placenta is posterior.

Transvaginal ultrasound can be safely used to diagnose and follow pregnancies suspected of placenta previa.

If a placental edge reaches or overlaps the internal os on a transvaginal ultrasound at under 24-weeks gestation, a follow-up exam in the third trimester is recommended. If the placental edge lies between 20 mm from the internal os and 20 mm of overlap at over 26-weeks gestation, an ultrasound should be repeated at regular intervals. Overlap of over 20 mm is unlikely to resolve and is highly predictive of the need for Caesarean section. When the placental edge is over 20 mm from the internal os, a trial of labour is appropriate. Between 0 and 20 mm for the os is associated with a higher Caesarean section rate.

For the individual patient, it is not possible to predict whether a bleed will occur or the gestational age, volume, or frequency of bleeding. A higher likelihood of bleeding is associated with a placenta that covers the os. Patients with placenta previa should be advised to avoid vaginal intercourse and exercise after 20-weeks gestation and decrease overall physical activity in the third trimester. These women can usually be managed as outpatients until vaginal bleeding occurs or until admission for Caesarean section. Other factors, such as shortened cervix, ability to get to a hospital promptly in an emergency, and availability of home support, may influence whether the patient is admitted to the hospital even if she is asymptomatic.

A course of antenatal corticosteroids should be given between 23- and 34-weeks gestation in women whose placenta covers the os.

Resources
1. Oppenheimer L, Society of Obstetricians and Gynaecologists of Canada: Diagnosis and Management of Placenta Previa. J Obstet Gynecol Can 2007; 29(3):261–266.
2. Lookwood C, Russo-Stieglitz: Management of Placenta Previa. www.uptodate.com/contents/management-of-placenta-previa. Accessed: May 18, 2012.

Answered by: Dr. Victoria Davis

8. Varenicline and Vascular Events

Does varenicline increase the risk for CV events in susceptible individuals?

Submitted by: Anonymous

There was initially some concern that varenicline may increase the risk of myocardial infarction; however, a recent meta-analysis of 22 randomized trials found no statistically significant difference in rates of CV events with varenicline or placebo (0.63% versus 0.47%).[1] This meta-analysis included 13 trials, which randomized patients with current or past CVD.

Varenicline is effective at helping patients stop smoking, and smoking cessation decreases the risk of myocardial infarction. At this time, there is no good evidence to suggest that we should avoid the use of varenicline in patients with CVD disease.

Reference

1. Prochaska JJ, Hilton JF: Risk of Cardiovascular Serious Adverse Events Associated with Varenicline Use for Tobacco Cessation: Systematic Review and Meta-analysis. BMJ 2012; 34:e2856.

Answered by: Dr. Bibiana Cujec

9. Persistent Fatigue after Treatment for Lyme Disease

? In a proven (serology) Lyme case with erythema migrans treated with doxycycline, should persistent fatigue be of concern?

Submitted by: Bruno Fafard, MD, Bromont, Québec

Many studies have shown that Lyme disease is treated successfully with antibiotics in most cases, and patients who have objective evidence of treatment failure are rare.[1]

A minority of patients treated for Lyme disease will have persistent or relapsing nonspecific symptoms (such as fatigue, musculoskeletal pain, and cognitive complaints) after receiving an adequate course of antibiotic therapy.[1] In the absence of another condition that would explain these nonspecific symptoms, such patients are classified as having post-Lyme disease syndrome.[1] Post-Lyme disease syndrome is estimated to occur 12 months after completion of therapy for erythema migrans in 10 to 20% of patients.[1]

Post-Lyme disease symptoms are worse in those with disseminated disease, greater severity of illness at presentation, and delayed antibiotic therapy, but they are not related to the duration of initial antibiotic therapy.[1] Children are less likely to develop post-Lyme disease symptoms.[1]

In many patients, these symptoms probably represent the natural evolution of response after therapy, as the percentage of patients reporting symptoms after antibiotic treatment decreases over time.[1] In other patients, a post-infective fatigue syndrome may be triggered by Lyme disease, similar to other infections.[1] Prolonged fatigue after infections is relatively common and can be disabling and persistent.[2] The mechanisms that result in post-infective fatigue syndrome are unknown, but it should also be noted that there is a significant background prevalence of similar symptoms in the general population.[1] Prolonged antibiotic therapy for post-Lyme disease offers no sustained benefit and may have potential serious adverse effects.[1]

References
1. Marques A: Chronic Lyme Disease: A Review. Infect Dis Clin North Am 2008; 22(2):341–360.
2. Hickie I, Davenport T, Wakefield D, *et al*: Post-infective and Chronic Fatigue Syndromes Precipitated by Viral and Non-viral Pathogens: Prospective Cohort Study. BMJ 2006; 333(7568):575.

Answered by: Dr. Ameeta Singh

10. Treating Mosaic Plantar Verrucae

What is the most effective treatment for mosaic plantar verrucae?

Submitted by: Katherine Allen, MD, Belleville, Ontario

When considering treatments for warts, one must always remember that most warts will clear spontaneously with time due to acquisition of natural immunity (primarily cellular).

At times, all plantar warts, whether mosaic or not, can be difficult to clear. A 2011 Cochrane report on topical treatments for cutaneous warts in randomized controlled trials suggested that salicylic acid had a definite, but modest, beneficial effect compared to placebo.

Aggressive cryotherapy was felt to be more effective than gentle cryotherapy but with increased risk of adverse effects.

Other treatments looked at included 5-fluorouracil, dinitrochlorobenzene sensitization therapy, intralesional bleomycin, intralesional interferon, photodynamic therapy, intralesional antigen, and duct tape. The evidence for the effectiveness of these treatments was limited, but it was suggested that they could be considered for warts that did not respond to safer treatments, such as salicylic acid or cryotherapy.

A randomized controlled trial of liquid nitrogen versus topical salicylic acid for cutaneous warts in primary care was published in 2010.[1] Salicylic acid was used as a 40% concentration in white petroleum jelly on a daily basis for 13 weeks. Liquid nitrogen cryotherapy (applied with a cotton applicator) was used every two weeks for 13 weeks with three serial applications per visit, each one used to produce a frozen halo of 2 mm around the base of the wart (usually 2 to 10 seconds per application). The conclusion of this study was that cryotherapy was the most effective treatment for common warts. However, for plantar warts, there was no difference in efficacy between cryotherapy, topical salicylic acid, and a wait-and-see approach after 13 weeks.

Therefore, there is no "most effective" treatment for mosaic plantar verrucae. However, in practice I would suggest using moderately aggressive liquid nitrogen cryotherapy every two weeks with salicylic acid used as a keratolytic agent applied nightly followed by paring with a pumice stone before the next application of the salicylic acid as an initial approach if the patient wishes treatment.

Reference

1. Bruggink S, Gussekloo J, Berger MY, *et al*: Cryotherapy with Liquid Nitrogen versus Topical Salicylic Acid Application for Cutaneous Warts in Primary Care: Randomized Controlled Trial. CMAJ 2010; 182(15): 1624–1630.

Answered by: Dr. Richard Haber

11. Genetics and Berry Aneurysms

Is there a hereditary component to berry aneurysms? If so, how common is it?

Submitted by: L. Jensen, MD, Burnaby, British Columbia

An aneurysm is an abnormal dilatation of an artery due to a weakness in its wall. Intracranial aneurysms are most commonly saccular, and, due to their shape, they are often referred to as "berry" aneurysms. Although it is not exactly known, genetic factors do play an important role in development of intracranial aneurysms. About 10% of the individuals with a subarachnoid hemorrhage have a family history of intracranial aneurysms. The patients with a family history are usually younger at the time of diagnosis and may have multiple and large aneurysms as compared to those without a family history. One in ten individuals diagnosed with an intracranial aneurysm usually has a first degree relative with the same condition. Furthermore, autosomal dominant polycystic kidney disease and some other rare hereditary conditions are increasingly associated with intracranial aneurysms. It is also known that subarachnoid hemorrhage is less common in Europeans than in those of African-American, Asian, and Hispanic descent.

Reference

1. Breimer LH: Genetics of Aneurysmal Disease: The Dogs that Did Not Bark. Angiology 2010; 61(3):233–237.

Answered by: Dr. Abdul Qayyum Rana and Mr. Abdullah Rana

12. Temporary Desensitization vs. Long-standing Tolerance

Further to the article on desensitization to *Hymenoptera* venom, can you explain the difference between temporary desensitization and immune therapy long-standing tolerance?

Submitted by: David Kohll, MD, Saskatoon, Saskatchewan

The difference between these two concepts highlights an extremely important issue, not only in the realm of venom allergy, but also in other forms of immunotherapy. This therapy has traditionally included treatment for allergic rhinitis and venom allergy but is now the focus of investigation for treatment of several forms of food allergy. Desensitization to any allergen implies a temporary state of nonresponsiveness to that allergen. Implicit in this definition is the requirement for ongoing regular exposure to that allergen to ensure nonresponsiveness. Simply put, desensitization means you are able to tolerate an insect sting, as long as immunotherapy is ongoing. It is as though the effector responses have transiently exhausted themselves, but no permanent underlying change in the immune response is noted. Drug desensitization protocols are available for those allergic patients requiring the medication in question, but, once stopped, the patient is again presumed allergic to that medication. However, the goal for immunotherapy treatment goes beyond this. The ultimate desired endpoint for immunotherapy is that of long-term tolerance (*i.e.*, the ability to tolerate exposure to that allergen indefinitely after treatment has been discontinued). Tolerance indicates a long-term (hopefully permanent) reduction in immune responsiveness, usually associated with specific and measurable changes in the immune response to that antigen (*e.g.*, an increase in antigen specific T-regulatory lymphocytes). Tolerance has been shown for venom immunotherapy, where long-term studies (up to almost 20 years) continue to demonstrate effective protection against venom stings in treated venom-allergic patients.

Answered by: Dr. Tom Gerstner

13. PPIs and Calcium Absorption

Do PPIs block absorption of calcium carbonate and/or calcium citrate?

Submitted by: Christina Fisher, MD, Toronto, Ontario

Calcium carbonate is an insoluble salt. For the calcium to be released and become available for absorption, it must be solubilized. An acidic environment is needed for optimal solubilization. Calcium citrate is more soluble, and its solubility is less dependant on gastric acid. Once solubilized, there is little difference in absorption between calcium carbonate and calcium citrate.

Reduced gastric acid, whether a result of conditions, such as pernitious anemia, or drugs, such as proton pump inhibitors (PPIs) or H2 blockers, may reduce calcium carbonate solubility. It is worth remembering that calcium carbonate contains 40% calcium (calcium carbonate 500 mg contains 200 mg of calcium), while calcium citrate contains only 20%.

Two recent reviews[1,2] sum up recent thoughts on PPI use and bone disease. They conclude that PPIs may put patients at a slight risk for fractures, but the evidence is not strong. No additional calcium supplements are indicated. PPIs, if needed, should not be discontinued.

References
1. Targownik LE, Leslie WD: The Relationship Among Proton Pump Inhibitors, Bone Disease and Fracture. Expert Opin Drug Saf 2011; 10(6):901–912.
2. Yang YX, Metz DC: Safety of Proton Pump Inhibitor Exposure. Gastroenterology 2010;139(4):1115–1127.

Answered by: Dr. Robert Bailey

14. Dalteparin and Alopecia

Can extended use of dalteparin cause cytotoxic effects, such as hair loss?

Submitted by: **Harsh Hundal, MD,** Toronto, Ontario

Dalteparin is a low molecular weight heparin that is used in the treatment and prevention of venous thromboembolism. Its main toxicity is the risk of bleeding, which depends on patient factors, such as other comorbidities and the duration of the use of this anticoagulant. Other side effects include heparin-induced thrombocytopenia (HIT), hyperkalemia, and anaphylaxis. Long-term use may be associated with osteoporosis. The risk of alopecia has been reported in case reports and very small case series. Apsner R, *et al*, reported that in four of five chronic hemodialysis patients with a clear temporal association between excessive hair loss and dalteparin experienced restoration of normal hair growth after the anticoagulation had been switched to citrate. Furthermore, one of these patients had a recurrence of alopecia soon after re-exposure to dalteparin.[1] Barnes C, *et al*, reported a potential association between alopecia and the administration of dalteparin in a child treated for sinus venous thrombosis. Given the rare reporting of alopecia with the use of dalteparin, one should seek other causes of hair loss in patients.[2]

References

1. Apsner R, Hörl WH, Sunder-Plassmann G: Dalteparin-induced Alopecia in Hemodialysis Patients: Reversal by Regional Citrate Anticoagulation. Blood 2001; 97(9):2914–2915.
2. Barnes C, Deidun D, Hynes K, *et al*: Alopecia and Dalteparin: A Previously Unreported Association. Blood 2000; 96(4):1618–1619.

Answered by: **Dr. Cyrus Hsia**

15. Medications Linked to Thrombocytopenia

What medications are commonly linked to thrombocytopenia, and at what point would you recommend stopping the medication causing this?

Submitted by: Leyana Saville, MD, Orléans, Ontario

There are numerous medications associated with thrombocytopenia, called drug-induced thrombocytopenia. Often, it is difficult to prove that such an association exists except through exclusion of other causes and showing a possible temporal relationship. Chemotherapy drugs are a common cause of dose-dependent myelosuppression and, hence, thrombocytopenia. Other common classes of drugs include antibiotics, antirheumatic drugs, and antiepileptic drugs. Particular drugs that are known to be commonly associated with thrombocytopenia include quinine, abciximab, and heparin.

Quinine-induced thrombocytopenia may be seen within a few days to a week of exposure and resolves just as quickly with discontinuation of the medication.

Abciximab-induced thrombocytopenia can occur within hours or days of exposure and resolve within days to weeks. These causes of thrombocytopenia are often associated with a range of clinical manifestations, from no symptoms to severe bleeding.

Heparin-induced thrombocytopenia (HIT), on the other hand, is associated with thrombosis and must be considered in any patient exposed to heparin or heparin products. HIT usually occurs 5 to 10 days after exposure to heparin products, with an associated drop by more than 50% in baseline platelet counts.

If a medication is suspected of causing thrombocytopenia, and the clinical scenario permits, then one should consider stopping the medication. If the patient requires chemotherapy, antiepileptic medications, or another medication that is potentially life-saving or that could lead to potential irreversible damage if stopped, then discontinuation may not be possible. Certainly, if a patient is having a major bleed, then the suspected medication should be stopped immediately with close follow-up. If HIT is suspected, then all heparin and heparin products must be stopped immediately.

While thrombocytopenia may be attributed to a possible medication or drug exposure, all attempts should be made to rule out other causes of thrombocytopenia in a patient. Consider consultation with a hematologist if in doubt.

Answered by: Dr. Cyrus Hsia

16. Screening for Pancreatic Cancer

Should we use abdominal ultrasounds to screen for pancreatic cancer in a vague epigastric pain patient? Do we have any data to show any benefit?

Submitted by: Do Truong, MD, Calgary, Alberta

Currently, there is no role for the routine use of radiological investigations or serum tumour markers (*e.g.*, CA 19-9) in screening the asymptomatic patient for pancreatic cancer. However, given that this patient has symptomatic epigastric pain, further work-up should be undertaken. Does this patient have any associated red flag symptoms, such as jaundice, anorexia, malaise, or unexplained weight loss or fatigue? Is there a late presentation of diabetes mellitus? If not, then abdominal ultrasound would be a reasonable initial imaging modality to assess for potential etiologies to account for this patient's symptoms. Of note, the sensitivity of abdominal ultrasound for detecting pancreatic tumours decreases with smaller tumour size. However, if this patient has associated symptoms of concern, then a CT of the abdomen would be preferable to better delineate and characterize the abdominal structures. Depending upon the clinical presentation and working differential diagnosis, other investigations, including endoscopy and/or endoscopic ultrasound (EUS), could be considered. Although there is no direct data demonstrating a benefit for abdominal ultrasounds in the setting of pancreatic cancer, certainly the possibility exists that earlier detection could render the patient a candidate for surgical resection, which would afford better outcomes overall compared with patients with unresectable pancreatic cancer.

Answered by: Dr. Roger Y. Tsang

17. Ankylosing Spondylitis and Uveitis

There is a high incidence of patients with ankylosing spondylitis developing uveitis. What are the signs and symptoms of uveitis, and how is it treated safely without causing complications?

Submitted by: Paul Stephan, MD, Scarborough, Ontario

Acute anterior uveitis occurs in 20 to 40% of patients with ankylosing spondylitis, more commonly in males. Patients typically experience unilateral eye pain and redness, photophobia, and blurry vision. In rare cases, involvement is bilateral. Urgent diagnosis is made by slit lamp exam where leukocytes can be visualized in the anterior chamber, where they are normally absent. If untreated, band keratopathy of the cornea can develop, as can the formation of synechiae between the iris and the lens of the eye.

Treatment should be started within 24 hours of presentation. For anterior uveitis, topical glucocorticoids, such as prednisolone acetate 1%, are first line agents. If there is an inadequate response, systemic glucocorticoids are added. Aggressive cases of anterior uveitis in patients at risk for visual loss may also require immunosuppressive treatments, such as mycophenolate mofetil, azathioprine, or methotrexate, which also act as steroid-sparing agents. Although there are no formal trials evaluating anti-TNF therapies, observational studies show significantly less episodes of uveitis in patients receiving anti-TNF therapy for ankylosing spondylitis. Note that posterior uveitis (seen in other autoimmune diseases, such as Behçet's) is treated in a different manner.

Answered by: Dr. Michael Starr and Dr. Alexander Tsoukas

18. Screening for Intracranial Aneurysms

My new patient, a 37-year-old male, tells me his mother died of a ruptured intracranial aneurysm. Should he have an MRI?

Submitted by: Noel Rosen, MD, Toronto, Ontario

Genetic factors play an important role in the development of intracranial aneurysms. About 10% of the individuals with a subarachnoid hemorrhage have a family history of intracranial aneurysm, and about 10% of the individuals diagnosed with an intracranial aneurysm usually have a first degree relative with the same condition. However, screening of patients with a family history of ruptured cerebral aneurysm is controversial. The Stroke Council of the American Heart Association does not recommend screening for aneurysms in patients who have only one first-degree relative with a ruptured aneurysm.[1,2]

In spite of serious consequences of rupture of cerebral aneurysms, screening asymptomatic individuals, those without risk factors or with acquired risk factors, such as smoking or alcohol abuse, does not appear to provide much benefit.[3]

Although several studies have suggested screening patients who have two or more family members with cerebral aneurysms, one of the analyses indicated that screening in these patients may not significantly reduce morbidity or mortality. Therefore, the decision on whether or not to screen for cerebral aneurysms in patients who have two or more first-degree relatives with subarachnoid hemorrhage should be made on a case-by-case basis.

References
1. Rinkel GJ, Djibuti M, Algra A, *et al*: Prevalence and Risk of Rupture of Intracranial Aneurysms: A Systematic Review. Stroke 1998; 29(1): 251–256.
2. Breimer LH: Genetics of Aneurysmal Disease: The Dogs that Did Not Bark. Angiology 2010; 61(3):233–237.
3. Bederson JB, Awad IA, Wiebers DO, *et al*: Recommendations for the Management of Patients with Unruptured Intracranial Aneurysms: A Statement for Healthcare Professionals from the Stroke Council of the American Heart Association. Circulation 2000; 102(18):2300–2308.

Answered by: Dr. Abdul Qayyum Rana

19. Overview of Ulipristal Acetate

Can you review ulipristal acetate — its use (mechanism of action and role in therapy) and side effects?

Submitted by: Anonymous

Ulipristal acetate is a selective progesterone receptor modulator (both antagonistic and agonistic action) with primarily antiprogestin activity. It can delay ovulation for up to five days and appears to be effective after the luteinizing hormone rise has begun, but not peaked, a time when levonorgestrel emergency contraception is ineffective.[1]

A meta-analysis of two trials of ulipristal acetate versus levonorgestrel found it at least as effective, if not more effective, than levonorgestrel with no difference in the side effect profile.[2]

Ulipristal acetate is indicated for emergency contraception in the USA and Europe. In Canada, the drug is under review by Health Canada but has yet to be approved.

Ulipristal acetate (30 mg orally) should be taken as soon as possible — within 120 hours of unprotected intercourse or contraceptive failure.

Adverse reactions include headache (< 20%), irregular menses (< 20%), and abdominal pain or nausea (< 16%).[3] Contraindications to ulipristal acetate include known or suspected pregnancy, and it is not indicated for pregnancy termination. Teratogenic effects have not been seen in laboratory animals, but no long-term data exists in humans.

References
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Answered by: Dr. Victoria Davis

20. Nonalcoholic Fatty Liver Disease

What is nonalcoholic fatty liver disease? How can it be diagnosed and treated?

Submitted by: Anonymous

Nonalcoholic fatty liver disease (NAFLD) is a very commonly found problem. It has increased in the Canadian population along with the increase in obesity. NAFLD is just that: simple fatty liver. However, 20% of the time the fat of NAFLD becomes inflammed and then the prognosis changes. This inflammation in the liver is called nonalcoholic steatohepatitis (NASH). NASH is of concern, because 10% develop cirrhosis without, or eventually with, decompensation, and about 7% develop hepatocellular carcinoma.

Evidence now links NAFLD/NASH to a list of problems, including CVD, diabetes, sleep apnea, hyperlipidemia, and polycystic ovaries.

The detection of NAFLD is easy. The most common presentation is an elevated alanine transaminase (ALT) level detected with routine screening that is then investigated with further blood tests and ultrasound or incidental fatty liver found on an abdominal ultra sound. NASH, on the other hand, requires a liver biopsy.

Therapy for both NAFLD and NASH includes lifestyle changes. Exercise and weight loss are the basic recommendations. Occasionally, bariatric surgery and pharmacotherapy play a role. Vitamin E, pioglitazone, pentoxifylline, and the statins have all been involved in clinical trials. These drugs occasionally appear to be beneficial, but the progression to fibrosis often continues. Larger therapeutic trials are needed, and, because of the extent of the problem, they are underway.

Obviously, controlling the associated conditions, such as diabetes and dyslipidemia, is important. Ultimately, there is no established therapy other than weight loss and exercise. Dx

Answered by: Dr. Robert Bailey