Answers to your questions from our medical experts

1. Rising Creatine Phosphokinase on Fenofibrate

Recently, a patient put on fenofibrate had a creatine phosphokinase (CPK) increase from 160 to > 600. Is this common? What management for triglyceride increase would be best? This patient is asymptomatic.

Submitted by: R. K. Edwards, MD, Coquitlam, British Columbia

A large trial on long-term fenofibrate therapy in patients with Type 2 diabetes involved 9,795 subjects, of which half took fenofibrate. Safety data showed that < 1% had CPK elevations between five to 10 times or more. Other causes of an increased CPK elevation should be checked or the patient can be carefully rechallenged to see if the rise occurs again. If the CPK continues to be significantly elevated other medications to lower triglycerides can be used, such as niacin.

Answered by: Dr. Vincent Woo

2. Endoscopic vs. Open Removal of the Prostate

What are the advantages of endoscopic vs. open removal of the prostate and what, if any, are the different indications for surgery?

Submitted by: Thomas Maxwell, MD, Hawkesbury, Ontario

Laparoscopic radical prostatectomy is becoming more and more popular as the demand from patients increases steadily. Although this remains somewhat debatable, the advantages of laparoscopic prostatectomy include:

- better vision for the surgeon,
- less pain,
- faster recovery and
- minimal incision size.

Cancer control and functional results (erectile function and continence) are similar.

Answered by: Dr. Hugues Widmer

3. Management Options for Gout

What are the best management options for intermittent gouty episodes in the renally impaired?

Submitted by: Valerie Rapson, MD, Barrie, Ontario

Management of gout in patients with advanced renal failure not on dialysis can be challenging. During acute flares, since NSAIDs are contraindicated, glucocorticoids should be used. Because of the adverse effects of corticosteroids, long-term use is not encouraged.

With regards to gout prophylaxis, the only therapy currently available is allopurinol for long-term uric acid reduction and colchicine for prevention of gouty flares until a steady state is reached. In the setting of renal failure, the adverse effects of these drugs tend to be more common. This is why they should be used with caution and at reduced doses adjusted to creatinine clearance with careful monitoring for adverse outcomes. In the Compendium of Pharmaceuticals and Specialties there are guidelines on allopurinol dosing based on creatinine clearance. However, these guidelines were developed years ago and never fully validated.

Studies have shown that strict adherence to published allopurinol dosing guidelines in renal failure may lead to suboptimal control of hyperuricemia.[1] Because the benefit of lowering uric acid in this population is felt to outweigh the risk of allopurinol hypersensitivity reactions, allopurinol should be titrated slowly and with careful monitoring, with a goal towards achieving normalization of serum uric acid.

Another method of modestly lowering uric acid in this population is with phosphate binders used to control hyperphosphatemia which also coincidentally binds uric acid.[2] Although this effect is modest and cannot be a substitute for allopurinol, their use may allow for lower doses of allopurinol to be used, thus reducing the risks of adverse effects. Phosphate binders should not be used in patients with normal serum phosphate levels.

References
1. Dalbeth N, Kumar S, Stamp L, et al: Dose Adjustment of Allopurinol According to Creatinine Clearance Does Not Provide Adequate Control of Hyperuricemia in Patients with Gout. J Rheumatol 2006; 33(8):1646-50.
2. Garg JP, Chasan-Taber S, Blair A, et al: Effects of Sevelamer and Calcium-Based Phosphate Binders on Uric Acid Concentrations in Patients Undergoing Hemodialysis: A Randomized Clinical Trial. Arthritis Rheum 2005; 52(1):290-5.

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

4. Seeds and Nuts and Diverticulitis

What about seeds and nuts and diverticulitis? I can't find any evidence for or against this old wives' tale.

Submitted by: Steve Sullivan, MD, Victoria, British Columbia

The pathogenesis of diverticuli in the colon is due to increased intraluminal pressure, abnormal motility and decreased dietary fiber. Most cases of diverticular disease are asymptomatic with only 15% to 20% developing inflammation (diverticulitis) or complications (*i.e.*, bleeding, perforations, abscess, fistulas and strictures). The pathogenesis of diverticulitis is uncertain, but the theory of diverticulitis revolves around a fecalith causing stasis or obstruction of the neck of the diverticuli. This may lead to bacterial overgrowth, local tissue ischemia and microperforations. Though it may be reasonable to surmise that corn, small seeds or nuts can get "stuck" in the narrow neck of a diverticuli, there is no evidence in the literature to support this. In fact, a high fiber diet is the recommendation for prevention of diverticulitis. Therefore, in my practice, I do not recommend avoidance of nuts or foods with seeds to patients with diverticular disease.

Answered by: Dr. Richmond Sy

5. Recommended Antihypertensive for Aortic Insufficiency

What is a good antihypertensive to use in aortic insufficiency? Why are calcium channel blockers often used?

Submitted by: Shanti Rao, MD, Windsor, Ontario

There is a lack of evidence for the use of vasodilator therapy in order to prevent progression of severe aortic insufficiency (AI) in patients who are asymptomatic with normal left ventricular function. There is some conflicting literature evaluating the use of specific vasodilators nifedipine or enalapril, which is perhaps why the use of calcium channel blockers (CCBs) has become "popular." To date, and despite these studies, there is no evidence that specifically treating AI with vasodilator therapy is helpful.[1] BP should be managed and the choice of medication (including CCBs) should be based on patient/physician preference and tolerability of the specific therapy.

Reference
1. Mahajerin A, Gurm HS, Tsai TT, et al: Vasodilator Therapy in Patients with Aortic Insufficiency: A Systematic Review. Am Heart J 2007; 153(4):454-61.

Answered by: Dr. Richard Sheppard

6. Significance of Sputum Colour

Does the colour of sputum aid in the diagnosis of respiratory infections?

Submitted by: Jerry Graner, MD, Toronto, Ontario

The significance of sputum colour has been investigated in the setting of acute exacerbation of chronic obstructive pulmonary disease (COPD). The presence of purulent sputum is predictive of a high bacterial load, increased likelihood of a positive sputum culture for bacteria and increased neutrophil numbers in sputum.[1,2] Therefore, sputum purulence during an acute exacerbation of COPD may help in selecting patients who will benefit from antibiotic treatment.[1-3]

References
1. Stockley RA, O'Brien C, Pye A, et al: Relationship of Sputum Color to Nature and Outpatient Management of Acute Exacerbations of COPD. Chest 2000; 117(6):1638-45.
2. Soler N, Agustí C, Angrill J, et al: Bronchoscopic Validation of the Significance of Sputum Purulence in Severe Exacerbations of COPD. Thorax 2007; 62(1):29-35.
3. O'Donnell DE, Aaron S, Bourbeau J, et al: Canadian Thoracic Society Recommendations for Management of Chronic Obstructive Pulmonary Disease—2007 Update. Can Respir J 2007; 14(Suppl B):5B-32B.

Answered by: Dr. Paul Hernandez

7. Stopping the Itch of Insect Bites

Any helpful tips with regards to treating the itch of insect bites (*i.e.*, mosquitoes, spiders, bees, *etc.*)

Submitted by: Katherine Abel, MD, Leduc, Alberta

When an insect bites the skin, a complex mixture of venoms and salivary proteins can trigger a local reaction.

For mosquitoes, the best treatment is preventative. Suggest a combination of protective clothing and use of insect repellants containing N,N-Diethyl-meta-toluamide (DEET). Concentrations should be lowest in children (six months and up) at 10% DEET to up to 30% in adults. Clothing, bed nets, camping nets are available that are treated with insecticide such as permethrin.

Medical treatment consists of antihistamines, soothing lotions, topical anesthetics and corticosteroids. Antihistamines used daily just before and after exposure to mosquitoes may reduce immediate and early symptoms. Menthol (0.25%) and camphor (0.25%) in a glaxol base can be applied to affected areas as needed to reduce itch (keeping this mixture in the fridge and applying cold may be even more soothing). Topical anesthetics can be used to provide temporary relief from extremely itchy local reactions. Mid- to high-potency topical corticosteroids can be applied to individual lesions twice daily for five to seven days. Try applying the steroid under occlusion (*e.g.*, under a piece of plastic wrap or a Tegaderm™ patch) for one or two nights and then open until resolved. If lesions persist, intralesional steroid injections (*e.g.*, triamcinolone acetonide 10 mg/ml) are helpful. Systemic corticosteroids are reserved for relief from extensive or severe reactions.

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

8. ARBs for Isolated Hypertension

Can ARBs be used as first-line treatment for isolated hypertension?

Submitted by: **Fawzi Mankal, MD,** Winchester, Ontario

ARBs are an effective, well-tolerated and safe class of drugs to reduce hypertension. Based on their demonstrated efficacy and tolerability in the landmark Losartan Intervention For Endpoint Reduction in Hypertension (LIFE) study, ARBs have been recommended by the Canadian Hypertension Education Program (CHEP) for first-line treatment of both systolic-diastolic hypertension as well as isolated systolic hypertension without concomitant conditions since 2003.

Patients with isolated systolic hypertension frequently require multi-drug therapy to achieve the currently recommended target systolic BP values of 140 mmHg in general and 130 mmHg in the presence of diabetes mellitus or renal failure from any cause. In this setting, ARBs can be combined with other classes of antihypertensive medications such as diuretics, long acting calcium antagonists or ß-blockers for synergistic BP-lowering effect.

All six currently approved and marketed ARBs in Canada come in a variety of dosages and in fixed dose combinations with a thiazide diuretic at no additional cost. This provides physicians with a great deal of treatment flexibility and patients with an extremely effective therapeutic option that favours long-term adherence and therefore maximizes the potential for CV disease prevention. Since their first introduction in 1995, ARBs have become the fastest growing class of antihypertensive medications prescribed in Canada.

Resource

1. Lindholm LH, Ibsen H, Dahlöf B, et al: Cardiovascular Morbidity and Mortality in Patients with Diabetes in the Losartan Intervention For Endpoint Reduction in Hypertension Study (LIFE): A Randomised Trial Against Atenolol. Lancet 2002; 359(9311):1004-10.

Answered by: **Dr. George N. Honos**

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9. Treatment for Peripheral Vertigo

What is the appropriate use of betahistine dihydrochloride in the peripheral vertigo?

Submitted by: Gregory Belchetz, MD, Brampton, Ontario

Betahistine dihydrochloride is marketed in Europe, Canada, Mexico, Australia and elsewhere around the world, as a specific treatment for Meniere's disease. No brand of betahistine is approved for sale within the US. Meniere's disease (episodic vertigo, tinnitus and deafness) requires audiometrically documented hearing loss, on at least one occasion and exclusion of other causes (including acoustic neuroma), according to the American Academy of Otolaryngology Head and Neck Surgery guidelines.

The pathophysiology of Meniere's remains illusive. As a result of this, medical treatment options are not clear. Meniere's disease or endolymphatic hydrops is believed to result from abnormalities in the quantity, composition and/or pressure of the endolymph within the inner ear. Betahistine dihydrochloride is thought to cause vasodilation in ischaemic areas of the inner ear. Therefore, any drug that increases blood flow to the organs responsible for producing endolymph should theoretically worsen hydrops. In addition, it seems counter-intuitive to treat patients with histamine, for a disease that is relieved by systemic antihistamines.

Despite its considerable use in England (113,000 prescriptions each month), specific guidelines are difficult to find. There is no consistent evidence in the literature supporting the use of betahistine dihydrochloride for the treatment of Meniere's disease. There are some centers in Europe that also use betahistine dihydrochloride for non-Meniere's peripheral vertigo; the evidence for benefit in this group of patients is even more limited. However, there is a large clinical trial currently underway (the Observational Study in patients suffering from recurrent peripheral vestibular Vertigo to Assess the effect of betahistine 48 mg q.d. on quality of Life and Dizziness symptoms [OSVaLD]), collecting data from North and South America, Asia and Europe on > 2,000 patients with peripheral vertigo. The results have not yet been published, but this trial may help direct prescribing habits for this group of patients that are hard to manage.

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

10. Best Antidepressant During Pregnancy

What is the best antidepressant to use in a pregnant, drug-withdrawing woman in a (residential) treatment program (*i.e.*, for cocaine, crystal meth, alcohol)?

Submitted by: Elizabeth Watt, MD, Abbotsford, British Columbia

The cessation of regular cocaine and/or amphetamines use is associated with relatively mild symptoms of depression, anxiety, anhedonia, sleep disturbance (insomnia or hypersomnia), increased appetite and psychomotor retardation; however, these symptoms decrease steadily over several weeks. No pharmacological agents reliably reduce the intensity of withdrawal, which usually does not include physiological disturbances as seen in opioids or alcohol withdrawal. Residential treatment is helpful for patients who experience intense craving to provide them with the appropriate psychosocial interventions that include psychotherapy. Residential treatment will also limit their access to cocaine and/or amphetamines which has specific adverse effects on:

- the health of the pregnant woman,
- the course of the pregnancy,
- fetal and early childhood development and
- parenting behaviour.

Symptoms of alcohol withdrawal include physiological disturbances, which if not managed properly, could lead to serious consequences including withdrawal seizures, hallucinations and delirium tremens, all of which could adversely affect the course of the pregnancy. Symptoms of alcohol withdrawal typically begin four to 12 hours after cessation of alcohol use, peak in intensity during the second day of abstinence and generally resolve within four to five days. Patients with mild to moderate withdrawal symptoms will respond to conservative measures in the form of generalized support, reassurance and frequent monitoring. Patients in moderate to severe alcohol withdrawal will require the use of thiamine, fluids and benzodiazepines. The literature is less clear about which specific benzodiazepine to use during pregnancy. Unfortunately all benzodiazepines are designated as category D in terms of fetal risk (*i.e.*, there is positive evidence for a human fetal risk, but the benefits from its use in pregnant women may be acceptable despite the risk).

Unless the diagnosis of a major depression has been established, there is no indication to give antidepressant medication to the pregnant, drug-withdrawing woman in a residential treatment program (for cocaine, crystal meth, alcohol). If an antidepressant is indicated, then selective serotonin reuptake inhibitors, such as fluoxetine or sertraline, would be a possible choice. They are designated as category C in terms of fetal risk (*i.e.*, the drug could be given only if the potential benefit justifies the potential risk to the fetus).

Resource

1. APA Practice Guidelines for the Treatment of Psychiatric Disorders, 2006. Drugs in Pregnancy and Lactation, Seventh edition.

Answered by: Dr. Hany Bissada

11. CT vs. MRI for Pituitary Adenoma

In the work-up for pituitary adenoma, which is the best, CT or MRI?

Submitted by: Karen Packer, MD, Cochrane, Alberta

Pituitary adenomas are tumours of the anterior pituitary characterized by size and cell of origin. These are typically benign tumours which may present with suprasellar symptoms or hormonal abnormalities. About 10% of the normal adult population have pituitary abnormalities on MRI scans that are compatible with the diagnosis of asymptomatic pituitary adenomas ("incidentalomas"). Most pituitary adenomas remain asymptomatic and do not require treatment. MRI imaging is the superior imaging procedure for work-up of pituitary adenoma. CT scans are a reasonable alternative and may be more timely and cost-effective to perform. However, the sensitivity of a CT scan is less than an MRI, particularly for very small microadenomas.

Answered by: Dr. Sharlene Gill

12. Efficacy of Imiquimod for Plantar Warts

Is imiquimod an effective treatment for plantar warts? When should it be used instead of liquid nitrogen?

Submitted by: Charles Cheng, MD, Vancouver, British Columbia

Imiquimod is a topical immune modulating cream that stimulates the innate immune system through toll-like receptors. The only official indications for imiquimod in Canada are for genital and perianal warts in adults, actinic keratoses and superficial basal cell carcinoma. Any treatment for warts must be tempered with the knowledge that most warts spontaneously resolve with time without treatment when the body eventually mounts an immune response to the HPV.

Treating plantar warts with imiquimod would be an off-labeled use of this medication as it is not officially indicated for plantar warts or in children, in whom most plantar warts are seen. However, if one chose to use imiquimod off-labeled for plantar warts, the major obstacle is the poor penetration of the cream through the thick hyperkeratinized plantar surface of the wart. Therefore, the efficacy is poor.

There are no controlled trials of imiquimod in plantar warts, but there are isolated case reports in the literature of response. Some of these cases involved using concomitant salicylic acid as a keratolytic to try to enhance penetration as well as using imiquimod under occlusion.

In view of the poor response of plantar warts to imiquimod, the cost of the drug and the fact that treatment is off-labeled, I would not recommend treating plantar warts with imiquimod and would consider liquid nitrogen to be much more efficacious.

Answered by: Dr. Richard Haber

13. Safety of Flu Shots in Infants

Since the flu vaccine is contraindicated if a patient has an egg allergy and eggs are not supposed to be introduced before one-year-of-age, how can we safely recommend flu shots as early as six-months-of-age?

Submitted by: Norman Blustein, MD, Richmond Hill, Ontario

Firstly, the flu shot is not contraindicated in patients with egg allergies. Influenza vaccines grow in chick eggs and the final product may contain very small amounts of egg proteins (large variation in egg protein content has been reported). Most studies have demonstrated safety of influenza vaccine administration in children with egg allergy,[1] with the caveat of some simple precautions. For those children who have suffered from systemic reactions in response to egg ingestion and have had a confirmed IgE mechanism established by radioallergosorbent test and/or skin testing, a protocol has been established in which skin testing to the flu vaccine is followed by a graded administration of the full vaccine dose.[2] In this way, almost all patients with an egg allergy may be immunized, even those with severe reactions to egg. In addition, it should be noted that egg allergy tends to occur in an older age group of kids (usually toddler/preschool) and not in the first six months of age, when milk is the predominant food allergen.

References
1. James JM, Zeiger RS: Safe Administration of Influenza Vaccine to Patients with Egg Allergy. J Pediatr 1998; 133(5):624-8.
2. Zeiger RS: Current Issues with Influenza Vaccination in Egg Allergy. J Allergy Clin Immunol 2002; 110(6):834-40

Answered by: Dr. Tom Gerstner

14. Commonality of Asymptomatic Pelvic Vein Thrombosis

How common is asymptomatic pelvic vein thrombosis following delivery?

Submitted by: James Goertzen, MD, Thunder Bay, Ontario

The incidence of asymptomatic pelvic vein thrombosis in the postpartum patient is unknown and therefore of uncertain importance. In a small study attempting to determine the frequency of deep vein thrombosis in moderate- to high-risk patients post C-section, using magnetic resonance venography, the rate of deep pelvic vein thrombosis was 46%; however, the clinical significance of this surrogate finding is unknown for obstetrical thromboprophylaxis.

Suggested reading:
1. Rodger MA, Avruch LI, Howley HE, et al: Pelvic Magnetic Resonance Venography Reveals High Rate of Pelvic Vein Thrombosis after Cesarian Section. Am J Obs Gyn 2006; 194(2):436-7.

Answered by: Dr. Victoria Davis

15. HPV Vaccine in Boys

Should boys receive the HPV vaccine?

Submitted by: Anonymous, Edmonton, Alberta

The current recommendation for the HPV vaccine is for girls aged 11 to 12; however, it can be given to girls as young as nine. The rationale for vaccinating young females before they are sexually active is because the vaccine is most effective in this population who have not been exposed to the four types of HPV included in the vaccine. The obvious question that arises is whether there is a benefit to vaccinating girls/women at risk, would there be such a benefit in vaccinating boys. Intuitively, this would make sense as there may be health benefits to preventing genital warts in men which may ultimately lead to penile and anal cancers. In addition, men may serve as a vehicle by which HPV is transmitted to women. Therefore, if boys/men are immune, the chain of transmission may be blocked. Unfortunately, however, it is not known whether the vaccine is effective in boys/men and hopefully within the next few years, the answer will be known.

Answered by: Dr. John M. Embil

16. Replacing an ACE Inhibitor with an ARB

A patient experienced facial angioedema on ACE inhibitors (after six years of use). Can this patient safely use an ARB?

Submitted by: Aloke De, MD, Westville, Nova Scotia

Angioedema secondary to an ACE inhibitor can occur after years of treatment. The mechanism is felt to be increased bradykinin because of decreased degradation. Angioedema is an ACE inhibitor class effect and is not drug specific. A patient who develops angioedema on an ACE inhibitor should not be exposed to any other ACE inhibitor in the future. Much less commonly, angioedema may also be secondary to ARBs. Losartan and valsartan have both been implicated in case reports. In a case series of 13 patients who experienced angioedema with losartan, three patients had previously experienced angioedema with an ACE inhibitor.[1] Angioedema due to an ACE inhibitor or an ARB may also be secondary to unmasking of hereditary or acquired deficiency of complement 1-esterase inactivator, which is another cause of kinin-mediated angioedema

The safest approach is not to use ARBs in a patient who has angioedema with ACE inhibitor. However, if the indication is compelling (*e.g.*, heart failure with left ventricular ejection fraction < 40%) an ARB should be used with caution.

Reference

1. van Rijnsoever EW, Kwee-Zuiderwijk WJ, Feenstra J: Angioneurotic Edema Attributed to the Use of Losartan. Arch Intern Med 1998; 158(18):2063-5.

Answered by: Dr. Bibiana Cujec

17. Diagnosing Diabetes in the Pediatric Population

How to diagnose diabetes mellitus in the pediatric population? Are the labs investigations and values the same as in adults?

Submitted by: Sakina Raj, MD, Calgary, Alberta

The diagnosis of diabetes in the pediatric population is made the same as in adults. The investigations are also similar for diagnosing Type 1 and Type 2 diabetes; however, Type 2 is much less common in children than in adults, although unfortunately the prevalence is increasing.

The diagnosis of diabetes in the pediatric population is made the same as in adults.

Answered by: Dr. Vincent Woo

18. Length and Dose of PPI Treatment for Reflux

How long and at what dose of PPI do you treat your patients who have extra-esophageal manifestations of reflux?

Submitted by: Jean-Pierre Souaid, MD, Ottawa, Ontario

The atypical manifestations of gastroesophageal reflux disease (GERD) are often very difficult to treat. Symptoms of coughing, asthma, hoarseness and chest pain have all been attributed to or exacerbated by acid reflux. The literature lacks controlled trials in the therapy of atypical symptoms of GERD and the bulk of the evidence for management is largely empirical. The studies that are published often fail to show improvement of symptoms with treatment compared to placebo. Most clinicians will use an empiric trial of high-dose PPIs at double dose for at least three months to assess response. The obvious shortcoming of this strategy is interpreting PPI treatment failure. The sensitivity of empiric therapy is proposed to be much lower in extra-esophageal manifestations compared to classic GERD symptoms. Furthermore, it is often difficult to prove that GERD is responsible for extra-esophageal symptoms even after pH monitoring studies or upper endoscopies, which are often normal.

Answered by: Dr. Richmond Sy

19. The Success of the Obturator Tape Procedure

How successful is the obturator tape procedure in the treatment of bladder prolapse and urinary incontinence?

Submitted by: Roshan Dheda, MD, Bradford, Ontario

The obturator tape procedure is very effective in the treatment of urinary stress incontinence, with a success rate of around 85% to 90%. Also, it is a minimally invasive technique that can be performed as an outpatient surgery. It is not a corrective measure used to treat prolapses; thus, it should be accompanied by another technique if the prolapse is of concern to the patient.

Answered by: Dr. Hugues Widmer

20. Chronic Inflammatory Demyelinating Polyneuropathy

What is the current treatment for chronic inflammatory demyelinating polyneuropathy (CIDP)?

Submitted by: Robert Ecclestone, MD, Langley, British Columbia

CIDP is caused by an abnormal immune response against particular epitopes on the Schwann cells of the peripheral nervous system. Unlike its more acute cousin, Guillain-Barre syndrome, it progresses continuously for more than two months. Because the illness is a manifestation of the immune system gone wrong, current treatments are based on interfering with the immune system's ability to attack peripheral myelin. At this time, there are three regimens that have been proven equally effective in the treatment of CIDP:

- IV immune globulin (IVIg, a pooled blood product),
- plasmapheresis and
- corticosteroids.

What guides treatment is usually very practical concerns, such as availability of regular treatment (which can be a problem with plasmapheresis) and side-effects (which can be a major problem with long term steroid use). For most people, the mainstay of treatment is chronic, usually monthly, administration of IVIg.

If these treatments are not successful, other immune suppressant agents have been tried in small trials, as well as interferon agents; however, there are no clear results at this time.

What is clear is that the earlier treatment is started, the better the response, no matter what treatment is used.

Resource
1. Koller H, Keiseiner BC, Jander S, et al: Chronic Inflammatory Demyelinating Polyneuropathy. N Engl J Med 2005; 352(13):1343-56.

Answered by: Dr. Inge Loy-English

21. Treating Osteoporosis in Patients with Renal Failure

Please comment on the treatment of osteoporosis in patients who have renal failure, both mild and moderate.

Submitted by: Anonymous

Treatment of osteoporosis in the setting of renal failure is challenging secondary to the metabolic abnormalities that are concurrent with renal disease and because of the poor excretion of the agents used to treat osteoporosis.

As glomerular filtration rate (GFR) declines, there are a number of metabolic bone conditions that may be present. These span a spectrum from mild-to-severe secondary hyperparathyroidism in early stages of chronic kidney disease (CKD), to the development of additional heterogeneous forms of bone diseases, such as renal osteodystrophy, each with its distinct bone histomorphometric characteristics. Osteoporosis can also develop in patients with CKD and end-stage renal disease for many reasons beyond age-related bone loss and postmenopausal bone loss.

The diagnosis of osteoporosis in patients with severe CKD or end-stage renal disease is not as clearly defined as it is in patients with post-menopausal osteoporosis. All forms of renal bone disease may result in increased fracture risk, or have low T scores. BMD alone has not been found to be a reliable indicator of increased fracture risk, particularly in a hemodialysis population. Gold standard for making the diagnosis of osteoporosis in this population of patients is bone biopsy with decreased trabecular bone formation.

In patients with moderate-to-severe renal dysfunction, first-line therapy centers around measures to minimize bone turnover and regulate calcium/phosphate homeostasis. The treatment of osteoporosis using bisphosphonates, selective estrogen receptor modulators, calcitonin, estrogen and anabolic steroids is controversial as they may decrease bone turnover and increase the development of adynamic bone disease or even osteomalacia. This is the population of patients that could benefit most from bone biopsy to exclude other renal related bone disease prior to considering therapy.

The use of bisphosphonates is generally safe if creatinine clearance is > 30 ml/min to 35 ml/min. The use with decreasing creatinine clearance is not well studied. There are some reports that bisphosphonates can be used in reduced doses in this population of patients, however the trial data is not available.

Resources

1. Ersoy F: Osteoporosis in the Elderly with Chronic Kidney Disease. Int Urol Nephrol 2007; 39(1):321-31.
2. Gal-Moscovici A, Sprague S: Osteoporosis and Chronic Kidney Disease. Semin Dial 2007; 20(5):423-30.

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

22. Investigating Angioedema During Pregnancy

What investigations should be done on a patient who presents with angioedema during pregnancy?

Submitted by: C. Lynde, MD, Markham, Ontario

It is important in pregnancy that treatment options consider the potential impact on the developing fetus and the mother, whereas investigations may be carried out in most cases in a similar manner as with non-pregnant individuals. The most common considerations for angioedema are allergic, infectious (acute), or chronic causes such as idiopathic, hereditary, complement disorders, collagen vascular diseases, or malignancy (acquired C1 esterase inhibitor depletion).

It is important in pregnancy that treatment options consider the potential impact on the developing fetus and the mother.

The presence or absence of urticaria is also very important, as both inherited and acquired forms of C1 esterase inhibitor deficiency occur without hives. The presence of hives would allow for consideration of various physical urticarias (cold, exercise, heat) or vasculitis causes (serum sickness, hypersensitivity vasculitides).

As in all cases, a detailed history and physical exam is essential, with the goals of categorizing angioedema and/or hives as acute or chronic (longer than six weeks) and vasculitic (lesion bruises are painful and last > 24 hours).

Considerations for investigations include:

- white blood cell count and differential,
- erythrocyte sedimentation rate,
- antinuclear antibody,
- stool for ova and parasites, or
- a skin biopsy if vasculitis is likely.

Complement studies and thyroid antibodies should also be done. Liver function studies and hepatitis serology may also be considered.

Women may commonly complain that urticaria exacerbates during menses and although immunologic reactions to endogenous hormones have been proposed, there is little evidence to support such a mechanism. However, hormones may certainly have a role in modulating the severity of symptoms. Specifically, pregnancy and OC use have been associated with exacerbations of hereditary angioedema, so the C1 inhibitor level and functional assay would be important to assess in a pregnant woman with angioedema without hives.

Answered by: Dr. Tom Gerstner

23. Treating Psychogenic Pruritis

What are the treatments for psychogenic pruritus?

Submitted by: **Alan Russell, MD,** Leamington, Ontario

Psychogenic pruritus is a diagnosis of exclusion. There are no primary lesions, but patients may develop lesions from scratching, such as excoriations and skin thickening. Sleep is rarely interrupted. Psychogenic pruritus may be associated with other psychiatric conditions, such as psychosis and delusions of parasitosis, depression and generalized anxiety disorder.

When approaching a patient with possible psychogenic itch, ensure that dermatological and systemic causes of itch have been thoroughly investigated. Dermatological causes of systemic itch include "winter itch," pruritus of senescent skin, infestations (lice, scabies) and drug eruptions (opiates, ASA). Systemic causes of itch to consider screening for include:

- Chronic renal failure
- Endocrine:
  - Diabetes
  - Hyperthyroidism
- Hematologic:
  - Iron deficiency
  - Hemochromatosis
  - Polycythemia rubra vera
- Infectious
  - HIV
  - Hepatitis C
  - Trichinosis
- Liver disease:
  - Obstructive biliary disease
  - Cholestatic liver disease of pregnancy
- Malignancy:
  - Lymphoma
  - Leukemia
  - Multiple myeloma
  - Carcinoid
  - Solid organ tumours
- Neurologic:
  - Peripheral nerve injuries
  - Post-herpetic neuralgia
  - Multiple sclerosis

Treating psychogenic pruritus is often more challenging than for other causes of itch. Topical therapies (*e.g.*, menthol, camphor) are rarely effective. Antihistamines can be tried and sedating antihistamines are helpful when taken at night if sleep is interrupted.

For itch that is not responding to the above strategies, consider other underlying causes, need for a psychiatric consultation and referral to a dermatologist, who may try novel agents that act on various pathways in the perception of itch. These agents include antidepressants (*e.g.*, Selective serotonin reuptake inhibitors, norepinephrine and serotonin enhancer-mirtazapine), anticonvulsants (*e.g.*, gabapentin) and opioid antagonists (*e.g.*, butorphanol, naltrexone).

See our recent review for details:
1. Lynde CB, Kraft JN, Lynde CW: Novel Agents for Intractable Itch. Skin Therapy Letter 2008; 13(1): 6-9.

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

24. Chelation Therapy

Are there any scientific studies on chelation therapy for coronary artery disease (CAD)/cerebrovascular accident?

Submitted by: Anonymous

IV infusion of ethylenediaminetetraacetic acid (EDTA), a lead chelating agent is called chelation therapy. Vitamins are commonly given as part of the treatment. There are many uncontrolled studies (involving a total of 5,852 patients) of chelation therapy in patients with CAD. It is difficult to draw any valid conclusions from these studies. There was no effect of EDTA on exercise duration or angiographic progression of CAD in two placebo-controlled studies with a total of 25 patients.[1] A randomized, placebo-controlled, double-blind Canadian study from Calgary showed no benefit of chelation therapy on brachial artery endothelial function in 47 patients with CAD.[2] There is no reliable evidence to suggest that chelation therapy is of benefit to patients with CAD or cerebrovascular disease.

There are many uncontrolled studies (involving a total of 5,852 patients) of chelation therapy in patients with CAD.

The risks associated with this treatment are substantial and include:

- renal failure,
- arrhythmias,
- tetany,
- hypocalcemia,
- hypotension,
- bone marrow depression,
- prolonged bleeding time,
- convulsions,
- respiratory arrest and
- auto-immune diseases.

Patients should be dissuaded from trying chelation therapy.

References
1. Ernst E: Chelation Therapy for Coronary Heart Disease: An Overview of All Clinical Investigations. Am Heart J 2000; 140(1):139-41.
2. Anderson TJ, Hubacek J, Wyse DG, et al: Effect of Chelation Therapy on Endothelial Function in Patients with Coronary Artery Disease: PATCH Substudy. J Am Coll Cardiol 2003; 41(3):420-5.

Answered by: Dr. Bibiana Cujec

25. Managing Acutely Increasing Creatinine

What are some ways to manage a patient with many comorbidities who develops an acutely increasing creatinine?

Submitted by: P. Sullivan, MD, Sussex, New Brunswick

Acute dialysis is often suggested to be the first step in the management of acute increases in creatinine or acute renal failure, but this can often be avoided with careful management of the comorbidities accompanying renal dysfunction.

A step-by-step approach can be summarized as follows:

- STEP 1: determine urgency of acute renal failure and initiate emergency management as necessary. This includes treatment of life-threatening hyperkalemia (*i.e.*, potassium > 6.0 mEq/L or EKG changes consistent with hyperkalemia) and volume overload/pulmonary edema
- STEP 2: achieve euvolemia. If a patient is volume depleted, administer IV fluid resuscitation to treat a pre-renal cause of acute renal failure
- STEP 3: achieve urine output. Foley insertion can be followed by diuretic administration and an abdominal ultrasound should be ordered
- STEP 4: search for reversible causes. Discontinue ACE inhibitors or ARBs; historically look for contrast, aminoglycoside antibiotic or NSAID use
- STEP 5: renally adjust medication dosages. Antibiotics, allopurinol and oral hypoglycemics often require dosage adjustments while Metformin should be held due to risk of lactic acidosis
- STEP 6: initiate a renal diet. A low potassium, low sodium, low phosphate diet should be initiated with a fluid restriction of < 1 L q.d.
- STEP 7: achieve fluid balance. If the oliguria develops, IV fluid should be limited to maintainence requirements plus the amount of urine output
- STEP 8: monitor carefully. Repeat electrolytes and creatinine frequently and continually assess volume status for signs of fluid overload
- STEP 9: avoid further insults. Hypotension, IV contrast, aminoglycosides and NSAIDs should be avoided as they worsen the renal injury
- STEP 10: indications for dialysis. Hyperkalemia refractory to medical treatment, severe acidosis refractory to medical treatment, uremic pericarditis or encephalopathy, overdose and volume overload refractory to medical treatment should prompt rapid consideration for acute dialysis

These management steps should be done in conjunction with consultation by a Nephrologist or Internal Medicine specialist.

Answered by: Dr. Manish M. Sood

26. Urologic Work-Up for Enuresis in a Child

Does a seven-year-old, otherwise healthy boy with normal blood and urine tests, suffering from enuresis, need a urological work-up before initiating medical therapy with desmopressin acetate?

Submitted by: Dennis Glubish, MD, St. Albert, Alberta

In a perfectly healthy patient suffering from monosymptomatic enuresis (incontinence present only at nighttime), only history, physical examination and urine analysis are sufficient before initiating therapy. If there is a history (of urinary tract infections, daily symptoms, constipation, *etc.*) or a physical examination shows signs of spina bifida, for example, or you suspect a urological or neurological anomaly, then a urological examination should be performed.

Answered by: Dr. Hugues Widmer

27. Reducing Scarring After Surgery

Are there any proven remedies that reduce scarring after surgery?

Submitted by: Barbara Campbell, MD, Kingston, Ontario

Scars develop over months after surgery and can be a major concern for patients. During any procedure that involves tissue apposition, scar formation can be minimized by proper technique and material selection (*e.g.*, using non-absorbable sutures and/or long-lasting absorbable sutures). Also, avoiding locations prone to scar or keloid formation such as the trunk, upper back, shoulders, neck and ear lobes is helpful when possible. Some patients have a disposition to keloid formation or a family history of excessive scarring and incisions should be kept to a minimum in these patients.

Post-surgery, scarring can be reduced in a number of ways. If scar looks hypertrophic or keloidal (*e.g.*, extends beyond wound margin), early intervention helps prevent growth of a scar. Massaging helps prevent excessive fibrosis. Hydration/occlusion or use of silicone gel sheeting applied daily for a half to full day for two months can improve scar appearance.

Avoid possible pigmentary changes to scars (*e.g.*, hyper/hypopigmentation) by strictly protecting the wound from the sun using strict avoidance, clothing blockage and sunscreen.

High-potency topical or intralesional steroids are helpful for hypertrophic or keloidal scars. Patients should be cautioned of corticosteroid risks including decreased wound healing, local telangiectasias and atrophy. Other options that may be helpful include dermabrasion one to two months post injury and laser therapy.

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

28. Lotions to Lighten Brown Spots

Are there any OTC lotions that will lighten solar "brown spots" on the face?

Submitted by: Steve Sullivan, MD, Victoria, British Columbia

By solar "brown spots," one is referring to solar lentigines, but flat seborrheic keratoses on the face can look identical.

Any treatment of solar lentigines would begin with sun avoidance and use of a SPF 30 sunscreen containing UVB and UVA protection.

I am not aware of any OTC treatments that have been shown to be effective in treating solar lentigines. The only OTC products that would be available are 2% and 4% hydroquinone-containing topical products, some also containing small concentrations of glycolic acid. These have not been scientifically shown to be effective in lightening solar lentigines.

The Pigmentary Disorders Academy reviewed treatment of solar lentigines in 2006. The treatments were divided into topical therapy and physical therapy. The consensus of the group was that first-line therapy for solar lentigines was ablative therapy with cryotherapy. Lasers were also felt to be an effective treatment.

Topically, a fixed combination of 2% mequinol and 0.01% retinoic acid was shown to be effective in lightening solar lentigines in double-blind, randomized controlled trials. Also, topical retinoids in the form of adapalene and tretinoin were felt to be effective treatments.

Resource
1. Ortonne JP: Treatment of Solar Lentigines. J Am Acad Dermatol 2006; 54(5 Suppl 2):S262-71.

Answered by: Dr. Richard Haber

29. Medroxyprogesterone Acetate and BMD

What is the evidence that use of medroxyprogesterone acetate can lead to osteoporosis and what guidelines do we give to a young woman with a normal diet?

Submitted by: D. Chambers, MD, Banff, Alberta

Medroxyprogesterone acetate is a contraceptive injection which suppresses estrogen levels. Studies have shown that women who use this injection have lower bone density and long-term users under the age of 21 had the lowest bone density, especially if they started at a very young age. However, it appears that bone density recovers when it is stopped and there are no studies that answer the question of whether its early use leads to fragility fractures later in life.

The World Health Organization has suggested that medroxyprogesterone acetate be used with caution in women < 18 and > 45 and that alternative means of contraception be considered if possible.

A young woman with a normal diet should be counseled regarding adequate vitamin D and calcium intake, regular weight-bearing exercise and to avoid smoking and excessive alcohol intake.

Regarding the need for BMD measurement, it is not practical or useful to recommend scanning all woman on medroxyprogesterone acetate. However, in some situations, BMD testing may be appropriate since the results may influence management decisions. For example, women who have other risk factors for osteoporosis may benefit from BMD testing so that those with a bone density that is already low can consider alternative methods of contraception. It may also be appropriate to test women using medroxyprogesterone acetate who are approaching menopause, since this is a time when risk of osteoporosis may be increasing.

Dx

Answered by: Dr. Michael Starr