1. ACE Inhibitors and Potassium Levels

Should patients on ACE inhibitors routinely have their potassium levels checked?

Submitted by: Roshan Dheda, MD, Bradford, Ontario

Clinically significant hyperkalemia is extremely rare when ACE inhibitors are prescribed to patients for the treatment of hypertension who have no prior history of renal dysfunction. Baseline creatinine and potassium is generally obtained in such patients as part of the routine laboratory work-up of newly-diagnosed hypertension. These values should probably be routinely controlled each time the dosage of the ACE inhibitor is increased, but additional routine testing thereafter is unnecessary in patients with stable renal function.

Patients taking ACE inhibitors for vascular prevention can only be managed in a similar manner. Patients with chronic heart failure tend to be seen much more frequently with regular monitoring of electrolytes and renal function, independently of whether they are taking an ACE inhibitor or not. They are also likely to be on diuretics which reduce the likelihood of ACE inhibitor-induced hyperkalemia.

Answered by: Dr. George N. Honos

2. High Sperm Count and Infertility

A 25-year-old male has been married for three years, but he and his wife have been unable to conceive. His sperm count is 293 million. Can the high count cause infertility?

Submitted by: Nagi Iskander, MD, Brookfield, Newfoundland

A high sperm count is > 150 to 200 million sperm. This is referred as polyspermia. Polyspermia *per se* is not associated with infertility unless it is accompanied with low sperm motility or asthenospermia. If the latter is present, augmenting the number of ejaculations should reduce sperm count and improve motility. This can be verified after augmenting the frequency of ejaculations and then by having a short period of abstinence of 24 hours before the new spermogram.

A high sperm count is > 150 to 200 million sperm.

Answered by: Dr. François Maufette; and Dr. Hugues Widmer

3. Treating Ascites

In the treatment of ascites, should one start with furosemide or spironolactone?

Submitted by: P. Hawley, MD, North Vancouver, British Columbia

Before treating ascites with diuretics, it is essential to determine the underlying cause. A positive history of risk factors, such as alcohol abuse or viral hepatitis, would support a diagnosis of cirrhosis, which is the most common cause of ascites. An abdominal paracentesis should be performed in all inpatients and outpatients with new-onset ascites.[1] In patients with cirrhosis, the serum ascites albumin gradient (SAAG) should be > 11 gm/L. A SAAG of < 11 gm/L does not usually respond to diuretics.[1]

In the treatment of ascites, furosemide and spironolactone should be started at the same time. The usual starting dose is 40 mg of furosemide and 100 mg of spironolactone.

In the treatment of ascites, furosemide and spironolactone should be started at the same time. The usual starting dose is 40 mg of furosemide and 100 mg of spironolactone.[2] The doses of both drugs can be increased every three to five days, maintaining the 40 mg:100 mg ratio to achieve weight loss. This ratio has been the most successful in maintaining normokalemia. Maximum doses are 160 mg of furosemide q.d. and 400 mg of spironolactone q.d. Combining these diuretics are more effective than using either agent alone; however, furosemide can be temporarily withheld in patients presenting with hypokalemia.

Spironolactone is an antiandrogen causing gynecomastia in men. Amiloride is a potassium sparing diuretic that is a good alternative. Amiloride, 10 mg, replaces 100 mg of spironolactone.

It is important that all non-pharmacologic interventions include the cessation of alcohol and a dietary restriction of sodium to < 2 gm q.d. Patients should also avoid taking NSAIDs that can result in fluid retention.

References
1. Runyon BA: Management of Adult Patients With Ascites Due to Cirrhosis. Hepatology 2004; 39(3):841-56.
2. Runyon BA: Care of Patients With Ascites. N Engl J Med 1994; 330(5):337-42.

Answered by: Dr. Robert Bailey; and Dr. Melissa Johnson

4. Testosterone Therapy and Sleep Apnea

Why is testosterone contraindicated in a patient diagnosed with sleep apnea?

Submitted by: P. L. Tham, MD, London, Ontario

Obstructive sleep apnea (OSA) is a common disorder related to a frequent cessation or marked reduction of airflow due to obstruction of the upper airway, despite continued respiratory efforts during sleep. OSA occurs predominantly in men. Testosterone therapy has been reported to be useful in the treatment of men with androgen deficiency, who have low testosterone levels, to induce and maintain secondary sex characteristics and to improve sexual function, muscle bulk and strength along with BMD.[1] However, along with other potential side-effects (*e.g.*, polycythemia, altered hepatic function and lipid profiles and the development or progression of prostate cancer) exogenous testosterone therapy has also been shown to induce or worsen OSA.[1] The mechanisms (*e.g.*, altered ventilatory drive or neuromuscular control of upper airway patency) by which testosterone affects OSA is unclear. Individuals treated with exogenous androgen therapy should be carefully monitored for the development or worsening of pre-existing OSA.[2]

References
1. Bhasin S, Cunningham GR, Hayes FJ, et al: Testosterone Therapy in Adult Men with Androgen Deficiency Syndromes: An Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab 2006; 91(6):1995-2010.
2. Yee B, Liu P, Phillips C, et al: Neuroendocrine Changes in Sleep Apnea. Curr Opin Pulm Med 2004; 10(6):475-81.

Answered by: Dr. Paul Hernandez

5. Men and the Transmission of HPV

Since HPV is known to be associated with cervical cancer and since it is thought to pattern as a STD, then what is the pathology in males who transmit the virus? Is there a male oncologic correlate from HPV? Is there an increased risk of HPV-related cancers in the partners of women with cervical cancer?

Submitted by: George Linn, MD, Kingston, Ontario

Male sexual partners are believed to be vectors for HPV infection. The exact nature and prevalence of HPV in males is unclear. The risk of HPV infection in men is believed to correlate with:

- their number of sexual partners,
- being uncircumcised and
- young age.

However, the prevalence of oncogenic HPV subtypes is much less common in males. There is no established male oncologic correlate from HPV (excluding squamous cell carcinoma of the anus which may affect both genders). The association of HPV with penile squamous cell carcinoma is not well established.

Presently, there is no data to suggest that male partners of women with cervical cancer have an increased risk of HPV-related cancers.

Answered by: Dr. Sharlene Gill

6. Appropriately Treating Major Depression

A 35-year-old male who is in good physical health and who takes no medications was diagnosed with depression. He also reports a sleeping disorder. What would be the most appropriate medication?

Submitted by: Constance Goulet, MD, Radisson, Quebec

Sleep disturbances, particularly middle and late insomnia, are common in a major depression and usually resolves with the successful treatment of the depression. Accordingly, the major depression should be treated using either a serotonin-norepinephrine reuptake inhibitor (SNRI), such as venlafaxine (up to 300 mg q.d.) or a selective serotonin reuptake inhibitor (SSRI), such as citalopram (20 mg to 60 mg q.d. p.o.), or escitalopram (10 mg to 20 mg q.d.).

If the insomnia problem is severe enough to warrant immediate attention, then the sedating antidepressant mirtazapine (15 mg to 45 mg q.h.s. p.o.) could be used. However, it does cause weight gain as a side-effect. Another alternative is to add trazodone (50 mg to 100 mg q.h.s. p.o.), or zopiclone (5 mg q.h.s. p.o.) to a SSRI or to a SNRI.

Answered by: Dr. Hany Bissada

7. Elevated Serum Insulin in Young Women

What is the significance of elevated serum insulin in young women?

Submitted by: C. Frederick, MD, London, Ontario

In general, I do not believe the measurement of insulin levels should be done in individuals and the significance of a single value is minimal. There is too much variability in a single measurement and the values may change quite dramatically depending on the time of day, menstrual cycle, time of last meal and many other factors.

In a large group of young women, higher insulin levels are most often found in a number of clinical situations, including:

- obesity,
- polycystic ovarian disease,
- acanthosis nigricans,
- Type 2 diabetes and prediabetes and
- those with a family history of diabetes,

etc.

There is large overlap with this population and the "normal" population.

Answered by: Dr. Vincent Woo

8. Urine Testing vs. Vaginal Swabs for Chlamydia

How would you compare urine testing with vaginal swabs for diagnosing genital chlamydia infection?

Submitted by: Parvinder Singh, MD, Markham, Ontario

A *Chlamydia trachomatis* (*C. trachomatis*) infection is relatively common and frequently asymptomatic. Screening is a more effective means of control than the investigation of symptomatic patients. Who and how to screen remain subjects for debate. Polymerase chain reaction methodology has replaced the unreliable and difficult methods of culturing the organism. While opportunistic screening is less cost-effective and only slightly more effective in finding cases than the screening of high-risk populations, it has become the standard of care.

Attempts to widen the net of opportunistic screening have resulted in the development of a number of less invasive techniques, including self- or physician-obtained low vaginal swabs, tampons and urine samples. Ninety-four per cent of first catch urine specimens were positive in samples identified as positive by the gold standard endocervical swabs. Patient- and physician-obtained vaginal swabs were both more effective than first catch urine samples.

The question then is whether casting a wider, but less effective net, is better and impossible to argue. Because of medical evidence, this question could have legal consequences if a diagnosis of *C. trachomatis* or genital chlamydia is missed when using an inferior means of identification.

Attempts to widen the net of opportunistic screening have resulted in the development of a number of less invasive techniques, including self- or physician-obtained low vaginal swabs, tampons and urine samples.

In summary, the test is effective and better than not screening but should not replace the endocervical swab when one can be obtained.

Resources

1. Goeree R, Jang D, Blackhouse G, et al: Cost-Effectiveness of Screening Swab or Urine Specimens for *Chlamydia Trachomatis* from Young Canadian Women in Ontario. Sex Transm Dis 2001; 28(12):701-9.
2. Schachter J, Chernesky MA, Willis DE, et al: Vaginal Swabs are the Specimens of Choice When Screening for *Chlamydia Trachomatis* and *Neisseria Gonorrhoeae*: Results from a Multicenter Evaluation of the APTIMA Assays for Both Infections. Sex Transm Dis 2005; 32(12):725-8.

Answered by: Dr. David Cumming

9. Cephalosporins and Penicillin Allergy

Please discuss the use of cephalosporins in patients with a penicillin allergy, both by history and by skin test.

Submitted by: D. William Moote, MD, London, Ontario

First and foremost, a detailed assessment is required to establish the true likelihood of an allergy to penicillin, including establishing the probable mechanism. In the case of IgE-mediated reactions to penicillin confirmed by skin testing, patients may still be eligible for a trial for a cephalosporin. The degree of cross reactivity between penicillin and cephalosporins is much less than previously thought. Retrospective studies of cephalosporin reaction rates in the 2000s shave shown only a 0.2% rate (2:1000) in patients with a history of penicillin allergy, compared with a 0.06% rate in non-penicillin allergic patients.[1] If the reaction to penicillin was moderate-to-severe, I would still consider a non-penicillin medication first. Otherwise, I would test the skin of the patient to the cephalosporin in question.

Although skin testing to cephalosporins is not standardized, a positive test would certainly lead you to an alternate choice. If the skin test is negative, then one could proceed with a "test dosing" procedure in a controlled setting over several hours.

Reference
1. Goodman EJ, Morgan MJ, Johnson PA, et al: Cephalosporins Can Be Given to Penicillin-Allergic Patients Who Do Not Exhibit an Anaphylactic Response. J Clin Anesth 2001; 13(8):561-4.

Answered by: Dr. Tom Gerstner

10. Intervention and the Delusional Patient

At what stage should one intervene in treating a patient who refuses to eat or drink anything because of paranoid delusional thinking?

Submitted by: J. Milliken, MD, Bridgewater, Nova Scotia

If the patient has refused eating or drinking for > 24 hours because of paranoid thinking and continues to refuse any intake because of persisting delusional thinking, then involuntary hospitalization is indicated to avoid medical deterioration due to dehydration and starvation.

In hospital, the patient will require the administration of anti-psychotic medication and, if necessary, may have to be declared incompetent to refuse treatment.

Answered by: Dr. Hany Bissada

11. Risk of Osteonecrosis of the Jaw

What is the risk of osteonecrosis of the jaw (ONJ) in patients taking bisphophonates?

Submitted by: Henry Docherty, MD, Kelowna, British Columbia

Lately, this issue has received alot of interest; however, it is important to put this into a reasonable perspective. ONJ is an avascular necrosis that may occur in the upper or lower jaw and has been linked to the use of bisphosphonates since 2003. Yet, the majority of these cases were in patients who had malignancies, usually breast or myeloma and who were receiving IV bisphosphonates. A dental extraction was often documented in these cases as the most common inciting event of ONJ. There have also been reports of ONJ associated with the use of oral bisphosphonates; however, Bilezikian[1] summarized the risk with conventional oral bisphosphonates and estimated the rate at 1:100,000 (*i.e.*, very rare).

Therefore, some general recommendations and comments would include:

- Advising patients that there may be a rare risk. Higher risk patients (*e.g.*, those with cancer, or who are undergoing IV therapy, a root canal or dental extraction) may consider completing dental work prior to initiating bisphosphonate therapy
- Suggesting the avoidance of invasive dental procedures, if possible, while on bisphosphonates
- A discussion between the physician and the treating dentist may help to alleviate any excess concerns
- Understanding that there is no clear evidence that stopping bisphosphonates prior to a procedure will have any impact; yet, some have suggested stopping for three months, if possible, in high-risk situations

This is an evolving story and will continue to be followed closely in the literature.

Reference
1. Bilezikian JP: Osteonecrosis of the Jaw: Do Bisphosphonates Pose a Risk? N Engl J Med 2006; 355(22):2278-81.

Answered by: Dr. Michael Starr

12. Risk Associated with Angioplasty

What is the risk associated with an angioplasty for a 53-year-old suffering from a mitral valve and blocked coronary artery?

Submitted by: Raouf Dimitry, MD, Lachine, Quebec

Complications of percutaneous coronary intervention (PCI) include:

- death (1%),
- NSTEMI, secondary to embolization of atheromatous debris, or
- side branch occlusion with biomarker elevation of more than three times above the limit of normal (15%),
- stroke (< 0.5%) and
- urgent coronary artery bypass grafting (< 0.5%).

In patients with stable angina, PCI is primarily indicated to improve symptoms refractory to medical therapy. PCI is much less likely to be technically successful if the coronary artery is chronically occluded.

If the patient has severe symptomatic mitral valve disease, then PCI is not indicated at all. The patient should have bypass grafting of any coronary arteries with stenoses of > 70% at the same time as mitral valve surgery. If the patient with mitral valve disease has atrial fibrillation and is on warfarin, this is usually stopped two to three days before cardiac catheterization and resumed after the procedure. There is a higher risk of local complications (*i.e.*, groin hematoma requiring blood transfusions) if the patient is on heparin around the time of cardiac catheterization.

Answered by: Dr. Bibiana Cujec

13. Tiotropium and Prostate Cancer

Tiotropium should not be used in benign prostatic hyperplasia (BPH), but can it be used in a patient with prostate cancer?

Submitted by: S. Budhoo, MD, St. Lawrence, Newfoundland

Tiotropium is a long-acting anticholinergic bronchodilator used in the management of chronic obstructive pulmonary disease. It works by antagonizing muscarinic receptors and produces smooth muscle relaxation. Common adverse effects mainly related to its antimuscarinic effects include dry mouth and/or throat irritation. Rarely (< 0.1% of patients) is treatment associated with:

- Urinary retention
- Constipation
- Palpitations
- Allergy
- Acute angle closure glaucoma

Precaution is advised for BPH patients. Prostate cancer, unless locally advanced, should not cause retention. Therefore, it should not be an absolute contraindication to tiotropium administration. Furthermore, a growing number of male patients are now being treated for lower urinary tract symptoms (whether related to BPH or not) with anticholinergic drugs, without significant risk of urinary retention.

For resources, please contact **diagnosis@sta.ca.**

Answered by: Dr. Hugues Widmer

14. Screening for Barrett's Esophagus

How often should patients be screened for known Barrett's esophagus?

Submitted by: Terry Fridhandler, MD, Calgary, Alberta

Patients with Barrett's esophagus have metaplastic replacement of the normal squamous epithelium with columnar epithelium above the gastroesophageal junction.[1] Barrett's esophagus is associated with gastroesophageal reflux disease (GERD) and is a risk factor of esophageal adenocarcinoma. Treatment of Barrett's esophagus should focus on the suppression of gastric acid and endoscopic surveillance for dysplasia.

To achieve maximum acid suppression, patients should be treated with a proton pump inhibitor for GERD rather than with other therapies, such as histamine receptor antagonists. Esophageal mucosal inflammation, due to poorly controlled reflux, can adversely affect the ability to detect dysplasia.[2]

The American College of Gastroenterology recommends that patients diagnosed with Barrett's esophagus initially undergo two surveillance gastroscopies to screen for dysplasia.[1] Although the interval between these studies is not clearly defined, six months to one year would be reasonable. Esophageal biopsies should be taken from the segment of Barrett's at 1 cm intervals in four quadrants.[2] If no dysplasia is detected, the patient should then continue to undergo surveillance at three year intervals.[1]

If dysplasia is detected, the mucosal sample should be examined by an additional pathologist for confirmation. If the dysplasia is low grade, the patient should have yearly surveillance endoscopies until no dysplasia is detected.[2] If the dysplasia is high grade, the patient should be referred to a gastroenterologist or a surgeon to discuss treatment options as they can be controversial. High grade dysplasia can be treated by esophagectomy, endoscopic mucosal resection or ablation, or intensive surveillance with surgical intervention, only when esophageal adenocarcinoma develops.

References
1. Vakil N, van Zanten SV, Kahrilas P, et al: The Montreal Definition and Classification of Gastroesophageal Reflux Disease: A Global Evidence-Based Consensus. Am J Gastroenterol 2006; 101(8):1900-20.
2. Sampliner RE, The Practice Parameters Committee of the American College of Gastroenterology: Updated Guidelines for the Diagnosis, Surveillance, and Therapy of Barrett's Esophagus. Am J Gastroenterol 2002; 97(8):1888-95.

Answered by: Dr. Robert Bailey; and Dr. Melissa Johnson

The American College of Gastroenterology recommends that patients diagnosed with Barrett's esophagus initially undergo two surveillance gastroscopies to screen for dysplasia.

15. Symptoms of Grave's Thyrotoxicosis

Recently, I diagnosed a patient with Graves thyrotoxicosis. Her initial presentation consisted mostly of abdominal symptoms, specifically nausea and vomiting. Weight loss and fatigue followed. Her nausea and vomiting settled with metoprolol while awaiting I-131 therapy. Are nausea and vomiting known symptoms of Grave's thyrotoxicosis?

Submitted by: Barbara Kinsah, MD, Lacombe, Alberta

The clinical manifestations of Grave's disease are myriad and can involve practically any organ system. As well, patients with Grave's disease are more likely to have other autoimmune disorders (*i.e.*, Addison's disease, diabetes mellitus, B12 deficiency, *etc.*). Grave's can also exacerbate existing medical conditions. Elderly patients may not present with the typical symptoms as do younger patients.

The GI manifestations are commonly:

- diarrhea or hyperdefecation,
- increased appetite,
- elevated transaminases and occasionally
- hepatomegaly and
- splenomegaly.

Anorexia can also occur in some patients and is seen more in the elderly. Nausea and vomiting are generally not associated with Grave's disease although, as mentioned, Grave's disease may exacerbate another underlying medical condition.

Answered by: Dr. Vincent Woo

16. Prognosis for Hodgkin's Lymphoma

What is the prognosis for stage IIIA Hodgkin's lymphoma in a 33-year-old male?

Submitted by: Sandi Frank, MD, Edmonton, Alberta

Based on the information provided, it is difficult to estimate. A number of factors may adversely impact the prognosis of Hodgkin's lymphoma, including:

- stage IV disease,
- > 45-years-of-age at diagnosis,
- male,
- hemoglobin < 105 g/L,
- white blood cell count > 15 $X10^9$/L,
- lymphocyte count < 0.6 X 10^9/L and
- albumin < 40 g/L.

The presence of up to three factors are associated with a 70% likelihood of being progression-free at five years time. Four or more factors are associated with a < 50% likelihood of being progression-free at five years time.

Answered by: Dr. Sharlene Gill

17. Treating Polymyalgia Rheumatica

What is the treatment for polymyalgia rheumatica?

Submitted by: Diane Giroux, MD, Montreal, Quebec

Patients with polymyalgia rheumatica (PMR) classically respond well and quickly to 10 mg to 20 mg of prednisone q.d. In fact, the dramatic resolution of symptoms is often used as a diagnostic measure. Few patients will not respond to this dose and may require an increased dose of steroids. For patients who are slow to respond to these doses of steroids, other etiologies for their symptoms, such as giant cell arteritis, or paraneoplastic syndromes, need to be considered.

For maintenance, patients should be maintained for two to four weeks on the effective dose after the aching and stiffness have resolved. Following this, the dose may be decreased every two to four weeks by approximately 10% to the minimum amount that is needed to maintain suppression of symptoms. At doses of ≤ 10 mg of prednisone q.d., it is advisable not to reduce the dose by > 1 mg to 2 mg per month.

Relapse is more likely to occur when the steroid is tapered too quickly. If recurrent symptoms develop and are accompanied by an elevation in erythrocyte sedimentation rate or serum C-reactive protein, then resumption or an increase of steroids is appropriate. The goal should be the eventual discontinuation of the steroids when symptoms resolve.

The length of treatment in total is often for one to two years.

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

18. When to Switch the Oral Contraceptive Pill

Is it worthwhile to switch the oral contraceptive pill when a patient develops melasma as a side-effect?

Submitted by: William P. Taylor, MD, Medicine Hat, Alberta

There is little in the current literature about melasma/chloasma (a brownish hyperpigmentation most apparent on the face) and the birth control pill. It is generally considered an estrogenic side-effect of pregnancy and, infrequently, of the birth control pill. Most of the literature deals with high-dose estrogen birth control pills.

There is no published literature to serve as a guide for managing contraceptive needs in the patient who presents with melasma as a complication of OC use. Changing gestagens would be of no value and the option of reducing the estrogen dose cannot be supported from the literature (or dismissed as ineffective). However, it is worth a trial of low estrogen OCs in the individual patient, but if there is no improvement within two to three months, then alternative forms of birth control should be contemplated. Dermatological treatment should also be considered.

Answered by: Dr. David Cumming