Managing Asthma During Pregnancy

How is asthma managed during pregnancy; in particular, which medications are safe?

Submitted by: Robert Bernstein, MD, Dorval, Quebec

The response of asthma to pregnancy is variable. Poorly-controlled asthma can have serious consequences for the developing fetus, including prematurity, low birth weight and increased mortality. Acute asthma exacerbations need to be prevented or treated aggressively when they do occur to avoid fetal hypoxemia. Therefore, the use of medications to control asthma is desirable, even in the face of concerns about potential side-effects.

The best studied medications in pregnancy include inhaled corticosteroids, β-2 agonists and theophyllines. These medications have not been shown to be associated with increased rates of fetal abnormalities. Pregnant patients with asthma should be made aware that the greatest risk to their baby is from poorly-controlled asthma rather than from the medications typically used to maintain good asthma control.

Resource

Answered by: Dr. Paul Hernandez

Are Internal Exams Effective With Pap Smears?

With pap smears, are the internal exams effective? What patient should have internal exams (i.e., what age group)?

Submitted by: Wayne Dong, MD, Valemount, British Columbia

A pelvic examination is usually performed in asymptomatic women in combination with a pap smear, STI screening, before commencing the OC pill, or hormone therapy, or at the patient’s request (who may think it screens a range of pathology, but particularly for ovarian cancer).

The prevalence of ovarian malignancy in a healthy patient population is low. The sensitivity and specificity of a routine pelvic examination as a screening test for ovarian malignancy are low and a routine pelvic examination cannot be justified from the literature as a screening test. Unfortunately, neither cancer antigen-125 blood tests nor ultrasound provide any better screening for ovarian cancer, but this is the nature of a disease which frequently remains asymptomatic until widespread metastasis has occurred. Nevertheless, providing that a patient understands the limited value of the examination, performing a pelvic examination whenever some other screening activity is undertaken can be useful.

For resources, please contact diagnosis@sta.ca.

Answered by: Dr. David Cumming
What are the troublesome side-effects of topiramate for adults with migraine?

Submitted by: Gaétan Lavoie, MD, Ste-Félicité, Quebec

The goal with any form of pharmacotherapy is to get the right medication to the right patient at the right time, with a minimum of adverse effects. An awareness of the potential adverse effects that may arise from the institution of a therapy must always be considered.

Topiramate is a broad-spectrum antiepileptic medication used as monotherapy or in combination for seizure disorders in both adults and children. It is also indicated for migraine prophylaxis in adults.

Possible troublesome side-effects that are documented in the literature include paresthesias, fatigue, anorexia, hypoesthesia, concentration changes, anorgasmia and nausea.¹⁻³ Many of the common side-effects are dose-related or are the result of a rapid dose titration.⁴ Paresthesias appeared to be dose-dependent and occurred in 50% of patients with doses > 100 mg q.d.¹ Concentration changes and weight loss also appeared to have a dose-dependent component to them, with more patients experiencing these side-effects at 150 mg q.d. vs. 50 mg q.d.¹ Interestingly, although anorexia has been reported to occur in only 8% to 15% of patients, up to 78% of patients will experience some weight loss with topiramate therapy.¹⁻⁵

Other common side-effects may also occur in a dose-independent fashion. For example, the occurrence of nausea in 9% to 11% of patients appears to be similar in patients receiving either 50 mg or 150 mg q.d.¹ Somnolence and dizziness are also thought to occur independent of the patient's dose.⁴ Topiramate has also been associated with more serious side-effects (i.e., hepatitis, liver failure, palpitations, cardiovascular changes and nephrolithiasis).⁶

In addition, there are numerous drug interactions to consider with topiramate. One is ethinyl estradiol which, when combined with topiramate, may result in reduced contraceptive efficacy (dose-dependently) as a result of the induction of estrogen metabolism.⁴,⁶ Moreover, since topiramate has been shown to inhibit the activity of the cytochrome P450 2C19 (CYP2C19) enzyme, caution should be taken if a patient is also receiving another medication that is a substrate of CYP2C19, such as omeprazole or diazepam.⁴ Ginkgo, a commonly-used herbal medicine, has been found to have a significant inductive effect on CYP2C19, which may also affect the effectiveness of topiramate.⁶,⁷ Such drug interactions are important to consider as they may impact the development and degree of side-effects experienced by the patient.

As such, full awareness of the patient's concurrent medical conditions, risk factors, tolerance to adverse effects and other medications (including OTCs and herbals) must be considered when completing a risk-benefit assessment prior to and during topiramate therapy.

For references, please contact diagnosis@sta.ca.

Answered by: Professor Joel Lamoure; and Ms. Jessica Stovel
4. Using Bisphosphonates: For How Long?

How long to continue bisphosphonates once a T-score is > -2.5?

Submitted by: Michael Yachnin, MD, Ottawa, Ontario

Bisphosphonates have been used for many years to treat osteoporosis and have an excellent efficacy and safety profile. In fact, there is now data out on 10 years of continuous bisphosphonate use and there does not appear to be a deleterious effect on bone quality. On the other hand, there is also a study that compared continuing patients on bisphosphonates for a total of 10 years, vs. discontinuing the medication after a period of five years of continuous use. Although BMD slowly decreased over time in the group who stopped taking alendronate (a bisphosphonate), there was no significant increase in fracture rates. This implies that perhaps some patients could consider a “drug holiday” after five years of continuous use.

Although there are no firm recommendations available, it may be reasonable to discontinue therapy after several years in patients who are no longer in a high-risk category for fractures. These patients could be carefully followed and treatment could be restarted if significant deterioration is noted.

Resource

Answered by: Dr. Michael Starr

5. When to Refer a Patient to a Nephrologist?

At which point should I consider referral to a nephrologist if a patient shows (on his blood work) a progressive increase in his serum creatinine?

Submitted by: Wayne Chang, MD, Calgary, Alberta

The Canadian Society of Nephrology nicely outlines timing for referral in chronic kidney disease. All patients who are at high-risk for kidney disease should be screened with an estimated glomerular filtration (GFR) measurement. Screening is commonly performed using the estimate GFR (eGFR) based on the Modification of Diet in Renal Disease equation which is less reliable for eGFR > 60 mL/minute.

For patients with an eGFR of < 60 mL/minute, focus should be on detecting reversible reasons for abnormal renal function, such as medications (e.g., NSAIDs), intercurrent illness, volume depletion, or obstruction. Furthermore, the eGFR should be repeated in two weeks and if it is < 30 mL/minute, a referral to a nephrologist is warranted. Patients with eGFR from 30 mL to 60 mL/minute should have optimization of their BP (target < 130/80 mmHg), reduction in their proteinuria (albumin-to-creatinine ratio < 40, protein-to-creatinine ratio < 60, with first-line agents being ACE inhibitors or ARBs) and assessments for cardiovascular disease. In this group, the inability to reach targets, reduce proteinuria or a continual decline in eGFR should be followed with a referral to nephrology.

For resources, please contact diagnosis@sta.ca.

Answered by: Dr. Manish Sood
6. BP and Lipid Targets for Glucose-Impaired Patients

For patients with impaired glucose tolerance, but not overt diabetes, do you target the same BP and lipid goals as a true diabetic (i.e., are these patients considered to be at very high-risk for atherosclerotic disease)?

Submitted by: Dr. Dina Taub, MD, Calgary, Alberta

Patients with impaired glucose tolerance do have an increased risk of cardiovascular disease compared to individuals with normal glucose levels; however, they do not have as high a risk as patients with diabetes. Therefore, for these patients, it is important to assess all the other risk factors to make your decisions with regards to lipid targets. At this juncture, BP targets would be the same as the non-diabetic population.

Answered by: Dr. Vincent Woo

7. Reasons for Post-Vasectomy Pain

What is the cause of post-vasectomy pain and how is it best treated?

Submitted by: K. R. Popowich, MD, Calgary, Alberta

There is a well-recognized condition that occurs among a small number of men after having a vasectomy known as the post-vasectomy pain syndrome. This syndrome can begin immediately and can continue for many months and even years after a vasectomy. Its frequency varies depending on the literature, but can be estimated to affect 4% of those having undergone a vasectomy. Most often, pain is mild and does not greatly impact daily activities. The main causes of this syndrome include:

- An inflamed post-vasectomy sperm granuloma aggravating the surrounding nerve endings
- Inflammation and swelling of the surrounding nerves (neuroma could develop)
- A congestive state in the epididymis from back pressure to the epididymis and testes from performing a closed-ended vasectomy
- A vasectomy carried out too close to the epididymis causing chronic pain and inflammation at the epididymis

This syndrome should not be confused with shorter-term pain (that can be caused by infection and post-operative inflammation) which resolves with appropriate medication and does not linger long enough to fall into the category of becoming a syndrome.

Generally, patience and mild analgesia, consisting of anti-inflammatory drugs, should be sufficient in treating the post-vasectomy pain syndrome. Nerve blockers or steroid injections (in the case of granulomas) can be of benefit. It is very rare that a vasectomy reversal is performed.

Answered by: Dr. Hugues Widmer
Cisapride has been withdrawn from the market for concerning cardiac reasons. What is the common etiology of problems? Are domperidone and metoclopramide soon to follow? All of these agents seem to be chemically unrelated. Do they all act through vagal pathways?

Submitted by: Robert C. Dickson, MD, Hamilton, Ontario

Cisapride was taken off the market in Canada in August 2000, following a number of reports of serious cardiac arrhythmias and sudden cardiac death. Forty-four incidents were reported in Canada, with 10 reports of death. Cisapride, a prokinetic, was used for the treatment of gastroparesis, refractory gastroesophageal reflux disease and intestinal pseudo-obstruction. Its primary mechanism of action involves enhanced secretion of acetylcholine at the myenteric plexus. It also has weak dopamine receptor blocking effects and serotonin-4 receptor agonist effects. However, it prolongs cardiac repolarization via effects on the cardiac potassium channels. The result is a prolonged QT interval.

The adverse reactions that ultimately led to cisapride’s recall were QT prolongation, ventricular tachycardia, ventricular fibrillation, torsades de pointes and sudden cardiac death. These events were more likely if an individual was taking other drugs metabolized by cytochrome P450 3A4 (CYP3A4) (the enzyme pathway responsible for the metabolism of cisapride), but also occurred in individuals not taking such drugs.

Domperidone acts mainly by blocking peripheral dopamine receptors. It has also been shown to prolong the QT interval and this effect can be compounded by taking other drugs metabolized by the CYP3A4 system. In their January 2007 Canadian Adverse Reaction Newsletter (CARN), Health Canada reported that they received nine domestic reports of heart rate and rhythm disorders potentially related to domperidone use between 1985 and 2006. These cases mostly involved patients with complex medical histories who took a number of other drugs. No deaths were reported, although the outcomes were unknown in four of the cases. Health Canada makes no mention of an impending recall, but according to their newsletter, they are working with manufacturers to update the product monograph to highlight the potential for arrhythmias.

Metoclopramide stimulates upper GI motility by an unclear mechanism, apparently by sensitizing tissues to acetylcholine. Its antiemetic properties are the result of antagonism of central and peripheral dopamine receptors. The main adverse reactions relate to extrapyramidal symptoms, including pseudoparkinsonism, acute dystonic reactions, tardive dyskinesia and akathisia. Cardiac side-effects (i.e., hypertension or hypotension and tachycardias or bradycardias) are not prominent. Health Canada has no CARN reports on metoclopramide.

Domperidone and metoclopramide will remain available as prokinetics and antiemetics. As with all drugs, they are best prescribed with knowledge of expected side-effects and drug interactions.

For resources, please contact diagnosis@sta.ca.

Answered by: Dr. Robert Bailey; and Dr. Parveen Boora
9. When to Test for *H. Pylori*

Should every patient that presents with symptoms of GERD or PUD be tested for *H. pylori*? If so, what is the best test in this situation?

Submitted by: Ardavan Assemi, MD, Ottawa, Ontario

Not every patient who presents with symptoms of gastroesophageal reflux disease (GERD) or peptic ulcer disease (PUD) requires *H. pylori* testing. The Canadian Dyspepsia Working Group issued recommendations in 2000 (and revised them in 2005) concerning the management of patients with upper GI symptoms. They suggest that all patients > 50-years-of-age, with a new onset of symptoms, require endoscopy (or other investigation if endoscopy is not available) as do those with alarm symptoms. Patients on NSAIDs with symptoms should stop the drug and reassess their symptoms. Should they have to remain on NSAIDs, then cytoprotection is recommended. Failure to respond to these measures mandates endoscopic assessment.

Patients with none of the above mentioned symptoms, who present with clinical features of GERD, such as heartburn or acid reflux, should be treated with acid suppressive therapy. Remaining patients should be tested for *H. pylori*. The gold standard for testing is a positive identification from endoscopic biopsy. However in patients not undergoing endoscopy, the urea breath test appears to be the most reliable. Where this is not universally available, some use the presence of *H. pylori* antibodies to establish whether the patient has been exposed to *H. pylori*.

Answered by: Dr. Paul Coolican

10. Can Tiotropium be Used in Prostate Cancer Patients?

Can tiotropium be used in a patient with prostate cancer?

Submitted by: S. Budhoo, MD, Bay St. Lawrence, Nova Scotia

Tiotropium bromide is an antimuscarinic-anticholinergic inhaled agent for the treatment of chronic obstructive pulmonary disease. There is no absolute contraindication to the use of tiotropium in a patient with prostate cancer. As per the product monograph, urinary retention or difficulty urinating have been reported with tiotropium therapy. Tiotropium may worsen symptoms and signs associated with prostatic hyperplasia or bladder neck obstruction; hence, it should be avoided in patients with these active symptoms.

There is no absolute contraindication to the use of tiotropium in a patient with prostate cancer.

Answered by: Dr. Sharlene Gill
11. Flashbacks: A Manifestation of PTSD

A severely abused man (age 50) continues to have flashbacks of being hit from behind, which cause fainting or brief lapses of consciousness. He is not neurologically impaired, nor does he have epileptic seizures. What to do?

Submitted by: Colin Leech-Porter, MD, Vancouver, British Columbia

This man seems to suffer from post-traumatic stress disorder (PTSD) related to severe physical abuse endured in the past. Recurrent flashbacks represent one manifestation of PTSD. Since a neurological etiology to the recurrent fainting and the lapses of consciousness has been ruled out, it is likely that they are manifestations of the PTSD, particularly because they happen when the patient is experiencing flashbacks.

In terms of management, ideally the patient should be referred to a competent therapist who specializes in providing therapy to abused victims, either in an individual or group therapy setting. Meanwhile, a trial on an antidepressant, such as mirtazapine (30 mg to 45 mg q.h.s p.o.), or extended-release venlafaxine (75 mg to 225 mg q.d.), may be helpful to temporarily reduce the frequency and intensity of the flashbacks until the patient is assessed by a psychotherapist.

The patient should be referred to a competent therapist who specializes in providing therapy to abused victims.

Answered by: Dr. Hany Bissada

12. IV Atropine Use in Atrial Fibrillation

If IV atropine is given to a patient suffering from atrial fibrillation, what will happen?

Submitted by: A. Guron, MD, Stephenville, Newfoundland

Atropine is an anticholinergic drug that increases sinus rate and atrioventricular nodal conduction. Patients who are in atrial fibrillation will have an increased ventricular rate (e.g., from 50 bpm to 80 bpm, or 120 bpm) with 0.5 mg to 3.0 mg of IV atropine. Atropine would be indicated as a temporary measure in a patient with atrial fibrillation and presyncope related to a slow ventricular rate (< 40 bpm). The effects of atropine wear off in 30 to 60 minutes and a temporary pacemaker is often required. If the patient is asymptomatic and has a very slow ventricular rate (30 bpm to 40 bpm), β-blockers, calcium channel blockers, or digoxin therapy should be decreased or discontinued.

Answered by: Dr. Bibiana Cujec
Reactions to peanuts are quite variable with symptoms ranging from a few hives on the face, or severe, as in respiratory distress and hypotension. The amount of peanut protein required to elicit reactions is equally variable, ranging from a few milligrams to several grams. Ingestion is the principal route for food allergens, yet some highly sensitive patients may develop severe symptoms upon skin contact and possibly inhalation.\textsuperscript{1} Examples of this phenomenon were brought to public attention a few years ago because of anecdotal reports that passengers who avoided ingestion of peanuts nonetheless experienced allergic reactions on commercial airliners that served roasted peanuts to other customers.\textsuperscript{2} Studies have also demonstrated that washing is an effective way to remove peanut protein from cafeteria tables and that airborne peanut allergens were undetectable in simulated real-life situations when participants consumed peanut butter, shelled peanuts and unshelled peanuts.\textsuperscript{3}

In addition, cutaneous contact with peanut butter, as well as the smell of peanut butter generally does not elicit systemic allergic reactions. In a study conducted by Simonte, \textit{et al},\textsuperscript{4} 30 children with documented peanut allergy were challenged by applying peanut butter to a small area of skin. None had systemic reactions. In addition, none of the children reacted to a surface coated with peanut butter (the smell was disguised), when breathing for 10 minutes, 12 inches away from the surface.

Should peanut become aerosolized (e.g., exposure to ingestion of large amounts of shelled peanuts in a contained area), reactions to particulate peanut “dust” is certainly possible, but reviewing the literature suggests that these reactions are not typically characterized as severe or anaphylactic, but rather as contact or upper airway in nature.

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Answered by: \textbf{Dr. Tom Gerstner}
14. About Ciclesonide

Please comment on ciclesonide.

Submitted by: Claude Roberge, MD, Sherbrooke, Quebec

Ciclesonide is a once daily inhaled corticosteroid (ICS) indicated in Canada for the maintenance treatment of asthma in patients ≥ 18-years-of-age. Several properties of ciclesonide (e.g., a high proportion of lung deposition, required drug conversion to active form by esterases in the lung, high protein binding and inactivation by first-pass metabolism in the liver) theoretically result in targeting the ICS to the lung, while limiting systemic bioavailability.¹

Clinical studies have demonstrated that ciclesonide is well tolerated, with low rates of local or systemic side-effects (e.g., oral candidiasis, hoarseness, suppression of hypothalamic-pituitary-adrenal axis) compared with other ICSs.²⁻⁴

Ciclesonide has comparable clinical efficacy to low-dose fluticasone or budesonide in terms of improving lung function and achieving asthma control²⁻⁴

The recommended dose range for ciclesonide is 100 mcg to 800 mcg q.d.¹ One limitation for the use of this drug is the current lack of availability of a combination ICS-long-acting β-agonist inhaler (containing ciclesonide) to which patients could be progressed if their asthma remained poorly controlled despite regular use of 400 mcg q.d of ciclesonide alone.

References

Answered by: Dr. Paul Hernandez

15. When to Alter Low Thyroid-Stimulating Hormone

Should a patient with a very low thyroid-stimulating hormone (TSH) (on thyroxine) have the dose altered if they feel fine?

Submitted by: Tracey Clemans-Gibbon, MD, Castlegar, British Columbia

Unfortunately, subclinical hyperthyroidism is not well studied.

Though a patient may feel “fine,” the known risks for low TSH are an approximately three-fold risk of atrial fibrillation in older adults and increased bone loss, with an increased risk of osteoporosis, especially in post-menopausal women.

For patients with low TSH, I slowly try to normalize the TSH into the lower part of the normal range.

Answered by: Dr. Vincent Woo
Should all symptomatic knee effusions be aspirated for therapeutic and diagnostic purposes? Is it appropriate to inject cortisone to prevent recurrence of the knee effusion?

Submitted by: Roshan Dheda, MD, Bradford, Ontario

Arthrocentesis of a symptomatic knee effusion can provide substantial analgesic benefit to the patient. In the setting of inflammatory arthritis, large knee effusions are slow to respond to systemic therapy, including steroids and patients may get more immediate benefit from aspiration. The synovial fluid can be analyzed and this may be of diagnostic value.

Corticosteroid injections in the knee are used in both osteoarthritis and inflammatory arthritis. Patients may receive substantial benefit for up to several months after an injection.

Patients with symptomatic knee effusions should have aspirations done both for diagnostic and therapeutic reasons. A synovial fluid analysis should include:
- culture,
- white blood cell count and
- crystal analysis.

Intra-articular corticosteroid injections can be very helpful. There is some evidence that aspiration of the effusion prior to injection of steroid prevents relapse in rheumatoid arthritis patients. There is no evidence for this in non-inflammatory arthritis, although these patients may still have substantial pain relief from aspiration.

Regarding the question of whether to aspirate the joint prior to cortisone injection, there is one study (of 147 patients) comparing arthrocentesis and injection vs. injection alone in the setting of rheumatoid knee effusions. Those patients who received aspiration and injection had significantly fewer relapse rates than those who were treated with steroids alone (p < 0.001).

There is no data on the population of patients with non-inflammatory knee effusions with regards to aspiration preventing relapse.

In summary, patients with symptomatic knee effusions should have aspirations done both for diagnostic and therapeutic reasons.

Reference

Answered by: Dr. Sabrina Fallavollita; and Dr. Michael Starr
Administering Clopidogrel Following Stent Implantation

How long is clopidogrel used for after percutaneous transluminal angioplasty (PTCA) and coronary artery bypass graft (CABG)?

Submitted by: Tim Capello, MD, Ottawa, Ontario

Since stents are deployed in > 90% of percutaneous intervention (PCI) cases, I believe the term PTCA (in regards to this question) should be replaced by PCI.

Recommendations published in 2005 regarding the use of clopidogrel for the purpose of recent stent insertion are as follows:

- Clopidogrel should be given for at least one month after bare-metal stent implantation (unless the patient is at increased risk of bleeding; then it should be given for a minimum of two weeks):
  - Three months after drug-eluting sirolimus stent implantation
  - Six months after drug-eluting paclitaxel stent implantation
  - Up to 12 months in all patients who are not at a high risk of bleeding

Of note, 325 mg of acetylsalicylic acid q.d. should be given concurrently with clopidogrel and may be decreased to 80 mg or 162 mg q.d. after:

- one month following a bare-metal stent insertion,
- three months following a sirolimus stent insertion and
- six months following a paclitaxel stent insertion.

To address this question more specifically, clopidogrel should preferably be administered up to one year following any type of stent implantation, if the patient is not at high-risk of bleeding.

Clopidogrel should preferably be administered up to one year following any type of stent implantation, if the patient is not at high-risk of bleeding.

With recent findings of increased incidence of late-stent thrombosis with drug-eluting stents, there is much debate in the interventional community as to how long clopidogrel should be administered. Recommendations may very well change in the near future as many within the cardiology community are already advocating lifelong clopidogrel administration after drug-eluting stent implantation in patients who are not at high-risk of bleeding.

On a side note, clopidogrel is not specifically recommended after CABG, unless indicated for other reasons.

Answered by: Dr. Igal A. Sebag
Ordering CT Scans for First Episode Psychosis Patients

What is the evidence for ordering CT head scans on first episode psychosis patients?

Submitted by: Janice Van Kampen, MD, Toronto, Ontario

Neuroimaging (CT or MRI scan of the head) is recommended in first psychosis patients who present with neurological signs and/or symptoms. Although some brain diseases can mimic the presentation of schizophrenia, it is rare that patients with first episode psychosis and no neurological findings will have an unsuspected neurological disease revealed by brain imaging with a CT or MRI scan.

The most common findings with CT imaging in first episode psychosis, with no neurological findings, is nonspecific ventricular and cortical sulcal enlargement which may be present in 30% to 40% of these patients.

Resource

Answered by: Dr. Hany Bissada

Fasting plasma glucose can have its ups and downs

People with diabetes have often found it difficult to keep their glucose readings consistent - even with excellent diabetes management habits. To make matters worse, many patients with inconsistent fasting plasma glucose levels can still have near-normal A1C results. This frustrating reality creates uncertainty for doctors and patients alike.

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