1. Proton Pump Inhibitors in Children

A 12-year-old female, who is otherwise healthy, has documented reflux not controlled with ranitidine. Are PPIs safe and effective in this age group?

Submitted by: John Seguin, MD, Edmonton, Alberta

In children, as well as in adults, there are clinical conditions (*i.e.*, severe esophagitis peptic ulcer disease or the eradication of *Helicobacter pylori)* in which proton pump inhibitors (PPIs) offer advantages over histamine (H) 2 antagonists. The relatively common use of acid inhibitors (PPIs and H2 receptor antagonists) in uncomplicated gastroesophageal reflux disorders, or in the prevention of NSAID/steroid gastropathy, is often unsubstantiated and should be limited to very specific situations. There are limited short-term side-effects with PPIs and they are rarely associated with diarrhea, nausea and vomiting. PPIs appear to be safe in the adult population and no significant long-term adverse effects have been conclusively documented. There are no long-term studies on the safety profile for chronic therapy of PPIs in children.

Answered by: Dr. Robert Bailey; and Dr. Justin Cheung

2. Best Hypoglycemic Drug for a Diabetic

Which is the best oral hypoglycemic drug that we can prescribe to a diabetic patient whose creatinine is > 150 µ/L?

Submitted by: S. Sundar, MD, Mississauga, Ontario

In a patient with significant renal insufficiency, the number of oral agents becomes more limited. An estimated glomerular filtration rate should be performed to better assess the degree of renal insufficiency, if not already done by the laboratory. Self monitoring of glucose levels should be performed more frequently.

Metformin use is contraindicated with significant renal dysfunction because of the rare risk of lactic acidosis.

Sulfonylureas must be used with extreme caution and the dose reduced or discontinued if renal failure progresses.

Repaglinide can be safely used in renal failure, but the dose should be watched carefully in patients on dialysis.

Rosiglitazone and pioglitazone can also be used in patients with renal failure, but increased edema may occur and must be monitored.

Finally, acarbose should be discontinued when the creatinine clearance is < 25 ml/minute. Insulin can always be used in patients with renal failure.

Answered by: Dr. Vincent Woo

3. Removing an Ear Wax Plug: Who Should Do It?

Is it safe to use a syringe and water to remove a wax plug in the external auditory canal or should we refer the patient to a specialist who has better instruments to do this technique, despite long wait times?

Submitted by: Fernand Arseneau, MD, Moncton, New Brunswick

The use of a syringe for removing wax and foreign bodies, by medical doctors, has been in use since the 1820s. Most FPs will syringe ears and many nurses are trained and competent in this technique as well. While I could find little literature to document the safety of this technique, the reality is that it is used safely throughout Canada by many health professionals.

The presence of wax should be confirmed by otoscopic exam and the patient should not have a history of ear drum perforation or mastoid surgery. In addition, the canal should otherwise be healthy. Some patients may need to soften the wax with oil for several days prior to syringing.

Most FPs will syringe ears and many nurses are trained and competent in this technique as well.

The technique is easily mastered and the results are instantly appreciated by the patient.

Answered by: Dr. Paul Coolican

4. Treating Advanced Liver Failure

What would you suggest for the symptomatic treatment of patients in the advanced stages of liver failure with jaundice?

Submitted by: Ronald Nicholson, MD, Summerside, Prince Edward Island

This question is quite broad and the answer depends on whether the liver failure is acute or chronic and the symptom itself, be it:

- pruritus,
- encephalopathy,
- bleeding, or
- ascites.

More information is needed. However, patients with advanced liver failure should be assessed for their candidacy for orthotopic liver transplantation. If this seems a viable option, timely referral to a transplant centre is mandated.

Answered by: Dr. Phil Wong; and Dr. Min Soo Song

5. Chronic Obstructive Pulmonary Disease Treatment Alternatives

A young woman with myasthenia gravis and chronic obstructive pulmonary disease (COPD) is unresponsive to steroids and ß-agonists. She finds that tiotropium bromide and ipratropium bromide benefit her COPD, but exacerbate her weakness from myasthenia gravis. What alternatives are available to treat her COPD?

Submitted by: Tom Greenfield, MD, Deep River, Ontario

Myasthenia gravis is a neuromuscular disease in which auto-antibodies are typically directed against nicotinic cholinergic receptors found in the neuromuscular junction. Inhaled anticholinergics (*e.g.*, tiotropium bromide and ipratropium bromide) are selective, competitive muscarinic cholinergic receptor antagonists that primarily exert their clinical effects on bronchial smooth muscle (*e.g.*, bronchodilatory). There are no reported effects of these agents on nicotinic cholinergic receptors; there should be little concern for their use in a patient with myasthenia gravis.

It is also unusual for a patient with COPD to be truly "unresponsive" to ß-agonists. It is important to address barriers to patient response, such as:

- adherence with prescription,
- ensuring good inhaler technique and
- appropriate dosing of the ß-agonist prior to abandoning this class of medication.

Clinical efficacy can best be assessed through patient symptoms (*i.e.*, reduced dyspnea and improved exercise tolerance) rather than through changes in lung function. Many patients with COPD do better symptomatically with a combination of a long-acting ß-agonist and inhaled corticosteroid in a single inhaler. An alternative class of medications is the long-acting, oral theophyllines. Use of this class of medications requires weighing the potential risks for toxicity and side-effects along with the need for monitoring blood levels with the benefit of mild bronchodilation when more safe inhaled bronchodilator medications exist.

Answered by: Dr. Paul Hernandez

6. Prognosis of T1 Tumours

What is the prognosis for T1 squamous cell carcinoma of a vocal cord treated with radiation? What is the recurrence rate?

Submitted by: Herbert L. Domke, MD, Victoria, British Columbia

High cure rates are possible for T1 tumours (tumours limited to the vocal cord[s] with normal mobility). Rates of local control with laryngeal preservation and cancer-specific survival exceed 95% at five years time, for patients with T1 glottic cancers based upon estimates from case-series and larger single-arm prospective studies.

Resource
1. American Society of Clinical Oncology Clinical Practice Guideline for the Use of Larynx-Preservation Strategies in the Treatment of Laryngeal Cancer. J Clin Oncol 2006; 24(22):3693-704.

Rates of local control with laryngeal preservation and cancer-specific survival exceed 95% at five years time.

Answered by: Dr. Sharlene Gill

7. Nut Allergy Manifestations

What are the manifestations of a nut allergy?

Submitted by: A. F. Turcotte, MD, Quebec, Quebec

The symptoms of an allergic reaction to nuts are similar to any IgE-mediated acute reaction that may occur in response to the exposure of any food, drug, or venom. An anaphylactic reaction is generally defined as a multisystemic or severe systemic reaction, that may include one or more of the following:

- skin (hives),
- respiratory (wheeze or stridor, cough),
- GI (emesis, abdominal cramping, diarrhea),
- cardiovascular (hypotension), or
- neurological manifestations (lethargy, sudden somnolence).

There is an age-related pattern, as children are more likely to suffer from severe consequences of respiratory compromise (*e.g.*, bronchoconstriction) as part of a severe allergic reaction, whereas adults will more likely suffer cardiovascular compromise (*e.g.*, hypotension). The history of any reaction to a nut that is felt to be IgE-mediated should be further assessed for confirmation and for education regarding avoidance measures and the use of an epinephrine auto injector.

Answered by: Dr. Tom Gerstner

8. Steroids for Ulcerative Colitis?

When are steroids used for ulcerative colitis?

Submitted by: Wendy Rosenthall, MD, Mississauga, Ontario

Steroids can be used for the acute exacerbation of ulcerative colitis to induce remission. Steroids should not be used as maintenance therapy to maintain remission because of the adverse effects of long-term use and also because it has been well documented that steroids are not effective in maintaining remission.

In patients with moderate-to-severe colitis, 40 mg to 50 mg of oral prednisone q.d. can be started and tapered over time.

Steroid enemas may be effective in patients with left sided (*i.e.*, distal to splenic flexure) mild-to-moderate colitis not responding to topical 5-aminosalicylic acid enemas.

In patients who appear to be steroid-dependent, consider starting immunomodulator therapy (*e.g.*, azathioprine or 6-mercaptopurine) to maintain remission.

Answered by: Dr. Robert Bailey; and Dr. Justin Cheung

9. Prophylactic Antibiotics, Children and Ureteric Reflux

For children with ureteric reflux, how long should we put them on prophylactic antibiotics?

Submitted by: Howard Liang, MD, Vancouver, British Columbia

Reflux management is a controversial topic in urology. Ongoing studies will help in deciding between surgery and surveillance with or without antibiotics. The resolution time of reflux in an individual patient is not clear and there is no evidence that prolonged use of antibiotics do more than reduce recurrent infections.

In newborn patients, it is reasonable to wait until approximately five-years-of-age, assuming that no intercurrent breakthrough infections occur. Beyond this age, the kidneys become less prone to scarring after pyelonephritis. Thus, some practitioners are withdrawing prophylaxis as the child approaches the age of four or five, or even earlier in boys that are properly toilet trained. After this age, boys with asymptomatic reflux will require little or no formal follow-up as long as lifelong attention to good bladder habits are reinforced. They are counselled to seek prompt medical attention, as well as reassessment of their reflux status, if pyelonephritis were to occur in the future.

Girls have traditionally undergone open surgical correction, even for asymptomatic reflux that fails to resolve by the age of five, on the premise that it will reduce maternal and fetal morbidity during future pregnancy; however, this is also controversial. Another way to proceed would be to stop prophylaxy at the age of four or five and operate on girls who have recurrent infections.

Answered by: Dr. Hugues Widmer; and Dr. Diego Barrieras

10. A Look at Post-Stroke Depression

Post-stroke depression. How to diagnose it and treat it and for how long post remission before stopping it?

Submitted by: Paul Stephan, MD, Scarborough, Ontario

Depressive disorders are probably the most common emotional disorder associated with a stroke. Approximately 15% to 25% of community-based samples of acute stroke patients and 30% to 40% of patients hospitalized with acute stroke have a clinically-diagnosable major or minor depressive disorder. Patients with left-sided lesions tend to manifest major depressive symptoms more frequently than those with right-sided lesions. Understandably, these depressive symptoms, if left untreated, will adversely interfere with the patient's ability to participate in rehabilitation programs; thus, reducing their potential for physical recovery.

In terms of diagnosis, studies have shown that, apart from weight loss and early morning awakening, all of the affective and autonomic symptoms of depression were significantly more frequent among stroke patients with a depressed mood than among stroke patients without a depressed mood. Therefore, the use of the *Diagnostic and Statistical Manual of Mental Disorders IV* criteria is valid and reliable to diagnose post-stroke depression in patients with a cerebrovascular accident.

In terms of pharmacological treatment, several randomized double-blind studies have been published on the efficacy of antidepressants treatment on post-stroke depression. The first placebo-controlled study confirmed the effectiveness of nortriptyline in the treatment of post-stroke depression (the dosage started at 25 mg q.d. and increased gradually up to 100 mg q.d., if it was well tolerated).

More recently, another placebo-controlled study that compared 10 mg q.d. and 20 mg q.d. of citalolpram to placebo confirmed its superiority to placebo, which suggests that selective serotonin reuptake inhibitors do have a place in the treatment of post-stroke depression.

In a two-year longitudinal study, a consecutive series of 103 acute stroke patients were examined for depression at their three, six, 12 and 24 month follow-ups. It was concluded that the natural course of major depression appeared to be between six months and one year, whereas the duration of minor depression was more variable and in many cases, the patients appeared to be chronically depressed. Accordingly, post-stroke depressed patients should remain on antidepressant therapy at least for one year and maybe longer, if clinically indicated.

Finally, psychological treatment, including group and family therapy, has also been reported to be useful in helping patients adjust and cope with their losses, impairments and the altered reality of their lives. However, controlled studies have not been conducted for these treatment modalities.

Answered by: Dr. Hany Bissada

11. Ankylosing Spondylitis Markers

Does a negative HLA-B27 rule out ankylosing spondylitis in a patient with sacroiliitis?

Submitted by: Christian Proulx, MD, Port Colborne, Ontario

Human leukocyte antigen (HLA)-B27 is present in about 95% of ankylosing spondylitis (AS) patients. The prevalence of HLA-B27 in the population of some countries is up to 8% or 9%. In actuality, only a small per cent of HLA-B27 positive individuals in a given population suffer from AS. Although it is a marker that we can measure routinely, HLA-B27 is thought to contribute only 16% to 50% of the total genetic risk. Therefore, other genetic and environmental factors may also play a role.

Sacroiliitis is the hallmark feature of the spondyloarthropathies (SPA), which include classic AS, but also reactive arthritis, psoriatic arthritis and arthritis associated with inflammatory bowel disease. HLA-B27 is not required for a diagnosis of SPA in patients who present with inflammatory back pain and who have other features or other diseases associated with SPA.

With this in mind, a negative HLA-B27 does not entirely rule out AS in a patient with sacroiliitis, but should prompt a search for other conditions associated with SPA (as mentioned above).

Answered by: Dr. Michael Starr

12. Lycopene and Indole-3-Carbinol: Chemoprevention?

What is your feeling about the use of indole-3-carbinol and lycopene for reducing the risk of cancer?

Submitted by: Andrew Broadway, MD, Quebec, Quebec

Lycopene is a plant-derived fat-soluble carotenoid with antioxidant properties. It is responsible for the yellow, orange and red colours of fruits and vegetables and is found largely in tomatoes. Epidemiologic data suggests an inverse correlation between tomato consumption and the risk of prostate cancer (more than two servings per week, tomato sauce preferred).

Indole-3-carbinol is an antioxidant found in cruciferous vegetables (*e.g.*, broccoli, cauliflower, cabbage). The data regarding its role in chemoprevention is limited and controversial.

Answered by: Dr. Sharlene Gill

13. Characteristics of Lewy Body Dementia

What are the diagnostic criteria for Lewy body dementia?

Submitted by: Tim Snell, MD, Oromocto, New Brunswick

This syndrome is characterized by visual hallucinations, Parkinsonism, fluctuating alertness and falls. Dementia may precede or follow the Parkinsonism. Patients with Lewy body dementia are highly susceptible to metabolic perturbations and in many cases, delirium is the first manifestation of the illness. In these cases, the delirium may be precipitated by an infection or other systemic disturbance. A delirium induced by L-dihydroxyphenylalanine, prescribed for Parkinson's disease, may be the initial clue for the diagnosis of dementia with Lewy bodies. Compared with Alzheimer's dementia, patients with Lewy body dementia tend to have a relatively better memory, but more severe visuospatial deficits.

Answered by: Dr. Hany Bissada

14. Should You Stop Bisphosphonates After 10 Years?

Is there any rationale for stopping bisphosphonates after 10 years?

Submitted by: Rita Khan, MD, Kitchener, Ontario

There is currently no consensus on when to stop bisphosphonates. The only evidence available to support discontinuing alendronate after five years comes from the recently published Fracture intervention Long-term EXtension (FLEX) trial, a five year extension of the Fracture Intervention Trial (FIT) where patients were randomized to alendronate or placebo five years after receiving alendronate continuously (JAMA, 2006). Patients in the placebo arm had a gradual decline in BMD and increased markers of bone turnover over five years, but their mean BMD remained the same or higher than levels 10 years earlier. The rate of fractures in either group was also not significantly different. Patients at the highest risk of fracture (those with FLEX baseline T-scores either < - 3.5, or below their FIT baseline) were excluded from the study.

These results indicate that in some women, stopping alendronate after five years may be reasonable. However, patients still at high risk of fracture, following treatment, should still continue therapy. On the other hand, the bone biopsy data available for bisphosphonates after up to 10 years of continuous use does not show any significant deleterious effects on bone quality. Therefore, there remains no clear recommendation regarding the length of time that patients can remain on a bisphosphonate. Dx

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