Referral Centres for Suspected Tropical or Infectious Diseases

1. For patients returning from vacationing in tropical countries, is there a comprehensive list of referral centres for suspected tropical or infectious diseases?

Question submitted by:
Dr. I. D'Souza
Willowdale, Ontario

It is not always easy to find clinics specializing in travel and tropical medicine. In particular, many travel clinics are really pre-travel centres, focusing on the sale of vaccines. They may have little or no specialized training in tropical illness, and they may not even have a doctor on site. There is no magic list that vets physicians' competence in any systematic way. In my opinion, the most reliable internet sites that list travel and tropical medicine physicians include the following; the American Society for Tropical Medicine and Hygiene www.astmh.org has a list of clinics affiliated with physicians active in the clinical group of the society. This is a relatively small list, but it generally includes highly trained physicians. The International Society for Travel Medicine www.istm.org also maintains a list of clinics, and the site allows you to choose between those providing pretravel and post-travel services. Again, the main requirement for listing is membership in this society. However, the list does indicate those members who have obtained the ISTM Certificate in Travel Health. The International Association for Medical Assistance to Travellers www.iamat.org provides a list of English speaking physicians worldwide, who have agreed to standardize consultation fees. This is a nonprofit organization that makes an attempt to screen the credentials of physicians on the list. You must become a member to access the list. In general, I would recommend that patients with more complex problems be referred to one of the clinics based in a university setting. These clinics are more likely to have highly experienced clinicians, as well as access to specialized diagnostic tests. In foreign countries, Canadian embassies or consulates can sometimes help travellers find reliable medical help.

Answered by:
Dr. Michael Libman

Managing Postcholecystectomy Diarrhea

2. How does one manage postcholecystectomy diarrhea?

Question submitted by:
Anonymous

The frequency of postcholecystectomy diarrhea (PCD) in patients is uncertain, with rates of up to 12% of patients being reported in the literature.[1,2] The pathophysiology of this condition is also unclear, and possible mechanisms include accelerated intestinal transit secondary to excessive luminal bile acids (liberated by the absence of a gallbladder reservoir).[3] However, bile acid concentrations in the aqueous phase of feces have been found to be below levels required for secretion in some patients with PCD.[3,4] Furthermore, bile acid malabsorption has also been observed in postcholecystectomy patients with a normal bowel habit.[3,4] Disregulation of ileal acid absorption through the fibroblast growth factor 19 mediated enterohepatic feedback has also recently been proposed as a possible mechanism of bile acid malabsorption and choleretic diarrhea, although a role for this in the pathogenesis of PCD has not been clearly defined.[5] Cholestyramine treatment, administered in divided dosages between 2 to 16 g per day, has resulted in symptomatic improvement in some patients with PCD in case series analysis, although the efficacy of this treatment has not been universal.[6,7,8] Given the uncertain pathogenesis of PCD, further data is needed to define specific therapies in the management of this condition.

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Answered by:
Dr. Theodore Xenodemetropoulos

Roflumilast in COPD Treatment

3.

Can you please review recommendations for the use of roflumilast in the treatment of COPD?

Question submitted by:
Dr. F. Ablarius
Côte Saint-Luc, Québec

Roflumilast is approved for use in patients with severe or very severe COPD who have a chronic productive cough and a history of exacerbations. It is given to prevent exacerbations and should not be continued if it has no impact on their frequency. Patients may find that roflumilast's side effects of nausea and diarrhea overshadow any benefit.

Answered by:
Dr. Robert Cowie

Probiotics in the Prevention of Repetitive Infections

4. What is the place of probiotics in the prevention of repetitive infections (otitis)?

Question submitted by:
Dr. Jocelyn Langlois Lac-Saint-Charles, Québec

Probiotics are live micro-organisms that provide a health benefit to the host. The beneficial effects are explained by stabilization of intestinal flora and modulation of immune function. The most widely used strains are *Lactobacilli*, *Bifidobacteria,* and *Saccharomyces boulardii* (nonpathogenic yeast).

It is known that probiotics reduce the risk of antibiotic-associated diarrhea, relieve symptoms of irritable bowel syndrome (IBS), and prevent necrotizing enterocolitis (NEC) in infancy. They may also reduce symptoms of upper respiratory tract infections. The most common reason for antibiotic use in children is acute otitis media (AOM). Studies on various pediatric populations that investigated oral intake of probiotics have included:

- Healthy children in day cares: The results showed no significant statistical difference between the studied groups
- Children prone to otitis: Inclusion criteria included at least four episodes of AOM per year or three episodes in the preceding six-months. The effects of probiotics were not strong enough to prevent infections in the studied population
- Healthy newborns: In one study, the incidence of AOM was 22% in the probiotic group and 50% in the placebo group in the first seven months of life. On the other hand, another study found no difference in the incidence of AOM in neonates until the age of eight months

Other studies investigated the use and effect of probiotic nasal sprays on AOM. The sprays were given for 10 days after the antibiotic treatment. In one study children were cured in the probiotic group (44%) versus in the placebo group (22%). However, Tano *et al* reported no long-term effects with probiotic nasal spray on AOM.

In summary, the present studies show conflicting data and contradictory results regarding the role of probiotics in the prophylaxis and treatment of otitis media. More studies are obviously needed, because it is difficult to draw valid conclusions at the present time.

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Answered by:
Dr. Ted Tewfik

Evaluating Patients with Elevated Serum Potassium

5.

Does a mildly elevated serum potassium level in asymptomatic pediatric patients with family history and chronic kidney disease need further investigation?

Question submitted by:
Dr. S. Echani
Edmonton, Alberta

The first consideration in evaluating patients who have had elevated serum potassium is the validity of the measurement tools used. Serum potassium is notoriously subject to collection issues, such that a mild degree of hemolysis will surreptitiously elevate the potassium concentration. This is a larger concern in children, due to potential difficulties in obtaining free-flowing venous blood in young children. Furthermore, electrolyte anomalies do not typically occur as an early sign of chronic kidney disease. Thus, a young child who has an elevated serum potassium and whose family has a history of chronic kidney disease should first be evaluated to determine if the serum potassium is actually elevated. If this is actually the case — and this would be very unlikely — other markers of renal function should be determined. In this context, there are some markers under development, such as cystatin C, that may be more useful than conventional markers, such as creatinine.

Answered by:
Dr. Michael Rieder

Epidural for a vWF Deficient Patient in Labour: Is it Safe?

6. Can a woman in labour with von Willebrand factor (vWF) deficiency receive an epidural?

Question submitted by:
Dr. Andrea Coholic
Timmins, Ontario

Von Willebrand Factor (vWF) deficiency encompasses a spectrum of diseases affecting up to 1% of the population. Autosomal dominant (AD) type 1 is the most common, accounting for 70 to 80% of affected individuals and resulting in a quantitative deficiency in vWF. Type 2, with four subtypes that are mostly AD, accounts for 25 to 30% of the disease and causes qualitative abnormalities in vWF. Type 3, an autosomal recessive disorder, causes severe disease with severely low levels of vWF. Depending on the manifestations and type of vWF deficiency, an epidural in labour may be considered. Pregnancy physiologically causes an increase in clotting factors, including vWF in the second and third trimesters, such that many patients have normal quantitative levels of vWF and factor VIII at term. Qualitative abnormalities, however, do persist. Whether an anaesthetist feels it is safe to administer an epidural for labour and delivery with a corresponding risk of spinal hematoma, depends on local and individual practices, the state of the patient's disease, and bleeding history. It is important to include the hematologist and anaesthetist in making plans for delivery in a centre where appropriate hematologic monitoring can be done. The Association of Hemophilia Clinic Directors of Canada will be publishing guidelines in the near future outlining the management of vWF patients in pregnancy and delivery. In summary, if vWF levels are normal at delivery and the patient has not had prior bleeding episodes or other hematologic problems, an epidural may be administered in labour. Prompt removal of the catheter, prior to the rapid post partum fall in clotting factors, is important to reduce the risk of bleeding.

Answered by:
Dr. Cathy Popadiuk and
Dr. Mary Frances Sailly vWF AHCDC Committee Member

Glucagon for Patients on Insulin

7.

Is it wise to have diabetic patients (on insulin) carry a glucagon pen in case of hypoglycemia with a reduced level of consciousness?

Question submitted by:
Dr. Alexis Thomson
Kelowna, British Columbia

Patients who have mild, symptomatic hypoglycemia and hypoglycemia awareness are generally able to treat hypoglycemic episodes through ingestion of 15 g of glucose, either in the form of glucose tablets or ingestion of approximately half-a- cup of orange juice, regular coke, *etc*. In patients who have had, or are at risk for, severe hypoglycemia (defined as requiring third party assistance, loss of consciousness, seizures, *etc.*), prescription of a glucagon pen can be life-saving, as a family member can administer glucagon when the patient is semi- or unconscious, and, thus, unable to ingest anything by mouth. I believe the glucagon kit costs about $80. It is not covered by the provincial formulary and insurance plans, and it expires after one year. I do not routinely prescribe glucagon to all my diabetic patients on insulin, but I do certainly discuss it with patients who are on an intensive insulin regimen or who have had issues with hypoglycemia in the past. It is essential to review and modify the treatment regimen in patients after an unexplained hypoglycemic episode to prevent recurrences.

Answered by:
Dr. Hasnain Khandwala

Treating Hirsuitism in a 15-year-old Girl

8.

How do you treat hirsuitism in a 15-year-old girl (no abnormal blood work, pelvic ultrasound is normal). She suffers from social isolation because of it.

Question submitted by:
Dr. Thomas Maxwell
Hawksbury, Ontario

Once primary causes for signs of hirsuitism are ruled out, specific treatments for the cutaneous signs of hypertrichosis should be discussed. Physical, simple methods of hair removal include shaving, waxing, plucking, electrolysis, and hair laser therapy. More aggressive cases can benefit from systemic therapy with spironolactone, finasteride, or antiandrogenic oral contraceptives.

Answered by:
Dr. Scott Murray

Treating *Dientamoeba Fragilis* with Liquid Alternatives

9.

How do you treat a 22-month-old female with *dientamoeba fragilis*? She is unable to tolerate oral metronidazole. She needs liquid medication

Question submitted by:
Anonymous

The choices for therapy of *Dientamoeba fragilis* are somewhat limited. The only two therapies available in Canada for *Dientamoeba fragilis* that are liquids are metronidazole for 10 days and iodoquinol for 20 days. While iodoquinol is a liquid alternative, it has a distinctly unpleasant taste. One key question in the therapy of *Dientamoeba fragilis* is whether *Dientamoebae* cultured from the stool represent pathogens or are co-conspirators, as there remains controversy as to the degree to which *Dientamoebae* cause symptoms as a single pathogen.

Answered by:
Dr. Michael Rieder

Switching Agents for Treating Depression Based on Weight Gain

10.

How can I switch, and should I indeed be trying to switch patients on olanzapine/ quetiapine/risperidone who have gained weight as a result of new atypical antipsychotics?

Question submitted by:
Dr. Julie Begin
Vaudreuil-Dorion, Québec

This is a large question that has challenged psychiatry since the metabolic syndrome became identified a little over a decade ago. Weight gain is multi-faceted in nature and may be linked to leptin changes, alterations in the satiety centre of the brain, sedation, genetics, *etc*. In clinical experience, weight is usually gained in the first six months of therapy, and depression based weight gain is commonly defined as gaining greater than 7% of the ideal body weight (IBW). Patients with a mental health disorder are at an increased risk of CVD, metabolic disorders, lipid abnormalities, and diabetes due to the condition itself. Adding more CVD risk factors, such as weight gain, will place the patient at even greater risk for microvascular, macrovascular, and endocrine disorders.

The majority of atypical antipsychotics may cause weight gain, although each to a different degree. Clozapine, olanzapine, and quetiapine are the most likely to cause weight gain. Risperidone may cause weight gain but to a lesser degree. Aripiprazole and ziprasidone are thought to be generally weight neutral. Weight gain is usually a drug specific issue, with increasing doses being a secondary factor.

In order to prevent metabolic syndrome and subsequent long-term negative outcomes, it is advisable to switch patients who have gained weight as a result of their atypical antipsychotic. Patients may be switched to one of the two newer, atypical antipsychotics that are relatively weight-neutral, ziprasidone or aripiprazole. The choice between ziprasidone and aripiprazole depends on the condition being treated, risk factors for QT prolongation, and axis 2 psychiatric comorbidities. If a patient is already at risk for QT prolongation due to medical conditions and/or medications, ziprasidone should be avoided, because it may also cause QT prolongation. Potential drug-drug interactions should also be considered. Ziprasidone is primarily a substrate of CYP 3A4, and to a minor degree, CYP 1A2. Aripiprazole is a substrate of CYP 3A4 and CYP 2D6.

Switching agents may be done through a variety of strategies including abrupt switching, cross tapering, or plateau cross titration. My clinical preference is to look at cross tapering, which may prevent the discontinuation syndrome associated with abrupt switches or negative additive adverse effects noted with plateau cross titration. Half-life, dose, active metabolites of the initial medication, and the new medications should be considered in switching.

Answered by:
Dr. Joel Lamoure
Contributor:
Professor Jessica Stovel

Symptoms of West Nile Disease

11.

How often is rash the presenting symptom in West Nile disease, and how common is it in Southwestern Ontario?

Question submitted by:
Dr. Klara O. Klein
London, Ontario

Serosurveys suggest that most infections are asymptomatic. The syndrome of West Nile fever is a non-specific, flu-like illness lasting a few days. Typical symptoms include fever, malaise, headache, and arthralgias. Published reports of outbreaks appear to describe varying incidence rates for other symptoms. A macular-papular or pale roseolar rash is reported in about 50% of cases, particularly in children. In some epidemics, conjunctival injection and generalized lymphadenopathy have been described as being common.

In recent years most Canadian cases were from the prairie provinces, and the number of reported cases dropped steadily, with only four cases reported in 2010. In 2011 the situation changed, with 110 cases reported, mostly from southern Québec and Ontario, especially the Niagara peninsula. Of the cases reported, 15 to 35% were neurologic West Nile disease. The rest of these cases had a variety of non-neurologic symptoms and a few were asymptomatic. Detailed information is available from the Public Health Agency of Canada at www.phac-aspc.gc.ca/wnv-vwn/mon-hmnsurv-eng.php.

Answered by:
Dr. Michael Libman

Should DREs be Performed on Female Patients?

12. Although digital rectal examination is common in males to check the prostate and the rectum, it is rarely performed in females. Should this be a routine procedure in females?

Question submitted by:
Dr. Robert Dickson
Hamilton, Ontario

The digital rectal examination (DRE) is a procedure commonly recommended and performed during the routine pelvic examination. Theoretical advantages of the rectovaginal examination (when compared with the standard bimanual examination), include allowing greater pelvic access enabling a better evaluation of pelvic viscera, and permitting palpation of abnormalities of the rectovaginal and uterosacral structures.[1,2] However, there is little evidence that this screening examination provides any clinical benefit in the asymptomatic female patient. Furthermore, evidence supporting the efficacy of DRE in screening for colorectal and prostate cancer in asymptomatic patients is also lacking. To date, there has been a conspicuous absence of data assessing the benefits (and test performance characteristics) of the DRE in the detection of colon cancer in the asymptomatic individual and, indeed, this examination has not been incorporated in the screening recommendations within any national guidelines, including those from the Canadian Association of Gastroenterology.[3,4] Despite the recommendation for both PSA and DRE in current Canadian prostate cancer screening guidelines, clear data for the benefit of screening DRE in the reduction of mortality has also not been demonstrated.[5,6,7] Some data has suggested the potential benefit of DRE in the detection of significant pathology in patients with rectal or prostatic symptoms, although definitive outcomes-based evidence within such heterogenous patient populations is presently lacking.[8] Ultimately, the evaluation of patients presenting with concerning symptoms may include the DRE as part of the initial assessment, but it necessitates the consideration of further evaluation, including appropriate specialist consultation and relevant diagnostic investigation.

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Answered by:
Dr. Theodore Xenodemetropoulos

Preventing the Spread of Genital Herpes

13.

A male patient inquires if he should be taking valacyclour for genital herpes to prevent sexual transmission from his partner. (He is unsure if he has herpes, but his partner does and she often has outbreaks).

Question submitted by:
Dr. Judi Marcin
Woodstock, Ontario

When an individual with no history of herpes infection (type 2) enters into a sexual relationship with an individual with a history of genital herpes, there is naturally some concern regarding acquisition of that STI. It has been shown that transmission to a noninfected partner is significantly decreased with suppressive valacyclovir therapy 500 mg q.d. (taken by the infected partner). Many persons who do not have outbreaks of genital herpes, may, in fact, be seropositive for herpes simplex 2 (HS2). Therefore, specific serology to determine HS2 positivity should be done before suppressive therapy is started. This test may not be readily available in all areas. As well, a benefit of decreased frequency of clinically apparent outbreaks has been seen during the course of suppressive therapy for the infected partner.

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Answered by:
Dr. Scott Murray

Differential Diagnosis for Periorbitol Edema

14.

I have a patient with periorbitol edema of the right eye. So far, his condition has stumped allergists, otolaryngologists, and opthalmologists. He has a normal CT finding of his head. Please suggest a diagnosis.

Question submitted by:
Dr. J.R. Brynjolsdon
Langley, British Columbia

The differential diagnosis of periorbital edema is very broad. It includes allergic, infectious, metabolic, autoimmune, neoplastic, and idiopathic etiologies.

The allergic examples could include angioneurotic edema, contact dermatitis, or insect bites. Infectious complications of sinusitis are preseptal lid edema, periorbital cellulitis, periorbital abscess, and renal diseases (glomerulonephritis, nephrotic syndrome, lupus, and lipid nephritis). Different orbital neoplasia, such as orbital pseudotumor, lacrimal gland, or palpebral soft tissue lesions may also be present. However, the different specialists that your patient has consulted must have eliminated most of these ailments. Another unilateral cause that I would rule out is Melkersson-Rosenthal syndrome (also known as cheilitis granulomatosa). This condition is characterized by recurrent or persistent lip edema, facial swelling (including periorbital tissues), furrowed tongue, and facial weakness or palsy. Most cases are sporadic, but familial occurrence suggests an autosomal dominant transmission. The syndrome is considered a local immune response and vasomotor disturbance affecting the vasa vasorum of the vessels supplying the facial nerve and surrounding structures.

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Answered by:
Dr. Ted Tewfik

Moulds in the Environment

15. What kind of air quality testing should I request for patients with medical conditions resulting from moulds?

Question submitted by:
Dr. Ailve McNestry
Vancouver, British Columbia

In general, the problem of moulds in the environment has been exaggerated. Certain moulds have the capacity to aggravate asthma, but their role in causing lung disease in people without asthma or seriously compromised immunity is not supported by the scientific literature. I do not encourage air quality testing for moulds. The companies that do the testing nearly always find something, and this then leads to expensive "remediation," which does not have any proven benefit.

Answered by:
Dr. Robert Cowie

Management of Benign Mastodynia

16. What is the best management of benign mastodynia?

Question submitted by:
Dr. Marrat Saida
Toronto, Ontario

Benign mastodynia (breast tenderness) can be cyclical, due to monthly hormonal effects, or non-cyclical, from the local chest wall or breast lesions. For benign mastodynia due to pendulous breasts, a firm support bra may be helpful. For mastitis, warm or cold compresses and antibiotics are recommended. Some patients improve after eliminating caffeine and fat from their diet or upon smoking cessation. Acetaminophen and NSAIDs can provide relief for most benign mastodynia, but, if not effective, a trial of the oral contraceptive pill or progesterone may counteract the hormonal effects of cyclic benign mastodynia in appropriate patients. Danazol is approved and effective for benign mastodynia, but it is associated with androgenic side effects. Tamoxifen, bromocriptine, and GnRH analogues are also rarely used in recalcitrant cases, but they are associated with unpleasant side effects and not approved for this indication. Most important in the management of benign mastodynia, particularly in the context of fibrocystic breasts, is confirming the problem is benign. Investigating any changes from the patient's usual symptoms is imperative. While breast cancer in women under 50 is uncommon, and usually not associated with pain, cases that are diagnosed during follow-up and treatment of benign mastodynia are very upsetting for the patient and physician alike.

Answered by:
Dr. Cathy Popadiuk

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