Consultant's Corner

Practical Answers To Your Everyday Questions

ACE Inhibitors and ARBs' in Congestive Heart Failure

1.

Do you recommend using both ACE inhibitors and ARBs in patients who have had congestive heart failure?

Question submitted by:
Dr. E. J. Framrok
Edmonton, Alberta

In the CHARM-Added trial[1], 2,548 patients with symptomatic congestive heart failure (HF) (NYHA class II or III with a mean LVEF 28%) all taking ACE inhibitors were randomly assigned to either candesartan or a placebo. Patients assigned to candesartan had a significantly lower incidence of the primary end point of cardiovascular death or hospitalization for HF (38% versus 42% adjusted hazard ratio 0.85; 95% CI 0.75-0.96). The overall rate of discontinuation of therapy was significantly higher for patients treated with candesartan (24% versus 18%) due to renal dysfunction or hyperkalemia.

2005 ACC/AHA guidelines recommend the following: 1) ARBs should be used in patients who are intolerant of ACE inhibitors; 2) ARBs may be used instead of ACE inhibitors among HF patients due to systolic dysfunction, particularly if the patient is already taking an ARB for another reason; 3) In addition to an ARB, if tolerated with a regimen including ACE Inhibitors and beta blockers in patients who have persistent NYHA class II or III HF and for patients who have normal renal function and low to normal serum potassium. Combined use of an ARB, and ACE inhibitors and an aldosterone antagonist should not be done routinely.

Reference

1. McMurray, JJ, Ostergren, J, Swedberg, K, et al. Effects of candesartan in patients with chronic heart failure and reduced left-ventricular systolic function taking angiotensin-converting-enzyme inhibitors: the CHARM-Added trial. Lancet 2003; 362:767.

Answered by:

Dr. Chi-Ming Chow

New Advances in Acne Treatment

2.

What are some of the new advances in acne treatment?

Question submitted by:
Dr. Abdalla Alrezaq
Edmonton, Alberta

There have been a few new therapies coming out. Topical dapsone is looking quite promising as well as some combination agents. The pairing of our 2 main comedolytic therapies topical retinoids and benzoyl peroxide has met with some success in trials and will be commercially available soon. There has been a proliferation of specialized light therapies, such as blue light, for acne. There had been evidence of efficacy but in my experience, the costs and ensuing heavy promotion of these therapies somewhat outweigh the benefits. Further developments of antiandrogenic contraceptives (such as drospirenone or cyproterone combined with ethinyl estradiol) have great benefits in female patients with hyperandrogenic states and acne.

Answered by:

Dr. Scott Murray

Distinguishing ADHD From Autism Spectrum Disorder (ASD)

3.

How does one distinguish ADHD from Autism Spectrum Disorder (ASD)?

Question submitted by:
Dr. Len Grbac
Edmonton, Alberta

While this may seem obvious, the distinction between ADHD and Autism Spectrum Disorder ASD is in fact more difficult to make than one would suspect, especially in young children. There are some overlapping symptoms. Indeed some authorities have suggested that ADHD be included in the range of Autism Spectrum Disorders, although this is not the conventional view. The differences between children with ASD and ADHD becomes more clear as they develop, with older children who have ASD becoming more withdrawn. In contrast, children with ADHD often develop (or are taught) coping skills which enable them to control impulsive behaviour and enhance their ability to interact in academic or social settings.

The temptation to diagnose very young children with ADHD should be avoided; the diagnosis of ADHD requires evaluation by clinicians who are experts in the evaluation of developmental and behavioural problems in children. This is important given overlapping symptoms in young children, e.g. young children with ASD and ADHD often have difficulties in peer relationships, but in the case of ASD it is due to difficulties in dealing with new situations and in the use of nonverbal cues. While in the case of ADHD, these problems are related to impulsivity. Similarly, while children with ASD and ADHD are both distractable, in the case of ASD this relates to objects and movements made by objects. On the other hand, in the case of ADHD this relates more commonly to people. The very different approaches to therapy of these two disorders mandates that the diagnosis be made with considerable thought and care.

Answered by:

Dr. Michael Rieder

Vocal Cord Tumours and HPV 1

4.

Is there a relationship between oral, pharyngeal, vocal cord tumours and HPV 1?

Question submitted by:
Dr. S Coyle
Edmonton, Alberta

More than 90% of head and neck cancers are of squamous cell histology and originate in the lip/oral cavity, nasopharynx, oropharynx, hypopharynx, and the larynx. Although tobacco and alcohol use are the primary risk factors for squamous cell carcinomas (SCCAs) of the head and neck, HPV a sexually transmitted infection, is also recognized as an independent risk factor for SCCAs of the head and neck. It is strongly associated with oropharyngeal SCCAs. The prevalence of HPV-positive cancers is approximately 36% and 51% for oropharyngeal cancers in general, and tonsillar cancers in particular, respectively.

The incidence of HPV-positiveoropharyngeal cancers is increasing, in parallel with a decline of HPV-negative cancers with the possibility that at one point practically all tonsil cancers will be HPV-positive, as in cervical cancer. HPV 16 accounts for a larger majority of HPV-positiveoropharyngeal SCCAs (86.7%) and HPV-positive oral SCCAs (68.2%). Conversely, HPV18 accounts for only 2.8% of HPV-positive oropharyngeal SCCAs and 17.0% of oral SCCAs. Other oncogenic HPVs are rarely detected in head and neck cancers. Although most of the evidence for a prognostic role of HPV comes from studies of cervical carcinomas, molecular and epidemiologic studies suggest that HPV-positive oropharyngeal cancers comprise a distinct disease entity that has a better prognosis.

Answered by:

Dr. Hay AlMarzouky
Dr. Ted Tewfik,

Bipolar Disorder in Teenagers

5. What is the prevalence of bipolar disorders in teenagers? Are their symptoms different from adults?

Question submitted by:
Dr. Dominique Lejeune
Edmonton, Alberta

The frequency of bipolar disorder is about 5% in adults who will have bipolar type two and 1 to 2% bipolar type one. However, there is a lot of variation in the numbers cited. Bipolar disease in teenagers appears to be much less frequent, with an incidence of approximately 1% of the representative population.

The youngest patient whose case I was involved in, was diagnosed as being bipolar at the age of five. This statement alone normally generates a lot of discussion, because individuals ask "how can one diagnose this?" How can it be differentiated from Oppositional Defiant Disorder, autism, ADD/ADHD or simply a "normal" evolution of development? Herein lies the challenge of treating individuals with bipolarity.

Bipolar disorder is a hereditary condition that is more clearly evident when a genogram is done for the patient and their family to address the condition of their mental health. There is evidence to support the belief that ADHD patients may have an increased likelihood of developing bipolar disorder, which may provide a Distant Early Warning system (DEW) for the clinicians and caregivers/family. At this point, under the Diagnostic and Statistical Manual, fourth edition, text revision (DSM-IV-TR), ADHD diagnostic criterion commencse at 7-years of age but it is anticipated that with the DSM-V-TR the age will be increased to the range of 11 to 13. As the incidence of ADHD goes down as age progresses, the frequency of bipolarity seems to increase, which may in part account for the links between these disorders. Regarding bipolarity and genetics, the condition is encoded and there is often an "activating event" that then results in the flaring or emergence of bipolarity. The activating event may be linked to puberty. As such, teenagers are more likely to have a clearer picture of true bipolarity, evidenced by manic and depressive components. Diagnosis requires careful observation over an extended period of time. This will also help prevent an improper diagnosis of depression and use of selective serotonin reuptake inhibitors (SSRIs) and serotonin/norepinephrine reuptake inhibitors (SNRIs), which are associated with switches into mania or increased suicidal tendencies within teenagers.

Literature reviews indicate that the manic symptoms that are displayed in adults who have bipolar 1 are somewhat muted as are their depressive symptoms. This adds to the complexity of diagnosis. Unfortunately, the symptoms displayed often overlap or look similar to drug abuse, schizophrenia, ADHD or delinquency according to the American Academy of Child and Adolescent Psychiatry (AACAP). AACAP provides a list of symptoms, such as mania described as severe mood changes, increase speech and distractability. In relation to depression in teenagers, changes in sleep, poor self-esteem, poor concentration, boredom or ahedonia (lack of pleasure from normally pleasurable activities) may be present.

Treatment options should be multimodal in nature. Cognitive Behavior Therapy (CBT), family involvement, plus day treatment support, or outpatient support should be indicated. The AACAP indicates treatment options such as lithium, mood stabilizers and atypical antipsychotics. Proper monitoring should be exercised as in the adult population, with emphasis on female patients, pregnancy risks and safety to the fetus with the use of most mood stabilizers and lithium. There are a couple of atypical antipsychotics that are indicated for depression in general and for bipolar depression more specifically. If depression can be reduced, it will help with prognosis in the long term and help prevent neurobiological changes (eg: hippocampal atrophy).

Multimodal therapies, careful observation of histories and judicious use of appropriate pharmacotherapy will, in part aid in the patient's success. This translates into school, family and work success for the patient.

Answered by:

Professor Joel Lamoure

Screening for Colon Cancer

6.

Which test for colon cancer has the longest protective interval?

Question submitted by:
Dr. Len Grbac
Edmonton, Alberta

Screening for colorectal cancer reduces mortality. Fecal occult blood tests, flexible sigmoidoscopy, double-contrast barium enema, and colonoscopy have been recommended as screening options for many years. Colonoscopy has the longest protective interval but there is limited evidence to determine the optimal frequency. We do know from one study that no cancers were found in follow-up colonoscopy testing in a group of 1,256 average risk patients who had had a negative screening colonoscopy five years earlier.[1] Another study followed a cohort of 35,975 patients who had a negative colonoscopy and compared the subsequent incidence of colorectal cancer to the general population.[2] The subsequent incidence of colorectal cancer was 72% lower than expected beyond 10 years. These findings suggest that a 10-year interval for colonoscopy following an initial negative study is an acceptable strategy for individuals at average risk.

References:

1. Imperiale et al. Five-year risk of colorectal neoplasia after negative screening colonoscopy. N Engl J Med. 2008 Sep 18;359(12):1218-24
2. Singh et al. Risk of developing colorectal-cancer following a negative colonoscopy examination: evidence for a 10-year interval between colonoscopies. JAMA. 2006 May 24;295(20):2366-73

Answered by:

Dr. Jerry S. McGrath

What Causes Thrombocytopenia

7. What are the causes of thrombocytopenia in the general population?

Question submitted by:
Dr. I D'Souza
Edmonton, Alberta

There are several causes of low platelet count or thrombocytopenia. By definition, thrombocytopenia is present when a platelet count falls below the reference range that typically falls between 150 - 450 x 10^9/L for most laboratories. This represents two standard deviations from the population mean platelet count and as such 2.5% of the population will have platelet counts less than this. The presence of platelet clumping should be ruled out, as this would suggest pseudothrombocytopenia, a phenomenon that occurs in approximately 0.1% of the population when peripheral blood is collected using EDTA as the anticoagulant. True causes of thrombocytopenia can then be classified into problems with marrow production, increased peripheral destruction, or sequestration. Decreased production includes exposure to marrow suppressive agents and bone marrow failure states from myelodysplastic syndromes, infiltration by leukemia or lymphoma, aplastic anemia, vitamin B12 or folate deficiencies and congenital disorders. Peripheral destruction is most commonly due to immune destruction such as idiopathic thrombocytopenic purpra (ITP). This is a diagnosis of exclusion after ruling out drug induced causes, associated autoimmune, or lymphoproliferative disorders, infections (such as HIV or Epstein-Barr Virus (EBV)), and other consumptive processes such as microangiopathic hemolytic anemias. One must also consider potential complications of pregnancy that cause thrombocytopenia in a fertile woman. Sequestration is seen in association with splenomegaly; most commonly in patients with portal hypertension secondary to liver disease.

Answered by:

Dr. Kang Howson-Jan and
Dr. Cyrus Hsia

Sitagliptin's Role in Diabetes Treatment

8.

What is the place of Sitagliptin's in the treatment of diabetes?

Question submitted by:
Dr. Danny Mckinnon
Edmonton, Alberta

Januvia (Sitagliptin) belongs to the relatively new class of hypoglycemic agents called the incretins. It inhibits the enzyme DPP-4 (dipeptidyl-peptidase 4) and thus leads to a prolongation of the effect of GLP (glucagon-like peptide). It leads to a stimulation in insulin release, inhibition of glucagon secretion and also inhibits gastric emptying. These effects seem to be glucose dependent and therefore do not occur in the presence of low blood glucose levels, thereby avoiding hypoglycemia. The effects on gastric emptying may also have a positive effect on satiety. They have a fairly good tolerability profile and generally appear to be free of side effects associated with other agents, particularly hypoglycemia and weight gain. They appear to be at least as effective as the other oral agents in terms of reduction in HbA1c. They are currently approved for use either as monotherapy or inpatients on metformin requiring additional therapy. I typically use it as a second-line agent after Metformin, as they lack the weight gain, fluid retention associated with the TZD's (Thiazolidinediones), and the hypoglycemia and weight gain of the sulfonylureas. I have also used it in triple and quadruple therapy; however this is an off-label indication.

Answered By;

Dr. Hasnain Khandwala

Contraception for Women Aged 45 to 50

9.

What is the best form of contraception for females aged 45 to 50?

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

Pregnancy in women over 44 is very uncommon and achieving a viable natural term birth is rare. That being said, pregnancy in women aged 45 to 50 is not impossible and consideration for birth control important. Usually in this age group, other gynecologic symptoms prevail such as menorrhagia and irregular menses. The progesterone IUD helps these problems and is an effective form of contraception that can last fo five years as menopause approaches. The oral contraceptive pill can also be used by women who do not smoke and do not have contraindications to it. Permanent forms of contraception such as a vasectomy in the partner, or tubal ligation are surgical procedures with corresponding surgical risks that should be carefully weighed in light of the extremely small risk of pregnancy in this age group. Ultimately, the decision is based on contraindications, side effects, and other symptoms and must be individualized to the patient and her circumstances.

Answered by:

Dr. Cathy Popadiuk

Fever in Patients who have had a Splenectomy

10.

If a patient has had a splenectomy, what do you do when they present with a fever (> 38°C)? Please answer for those that have been properly vaccinated and those who have not.

Question submitted by:
Dr. Ilona Grymonpre
Edmonton, Alberta

Although splenectomised patients may have deficits involving multiple immunologic pathways, the most serious problem involves their reduced ability to clear organisms whose capsules are important virulence factors. The most common of these by far is the pneumococcus, and pneumococcal sepsis, which may be fulminant and recurrent. Vaccination is probably helpful, but only some serotypes are covered in our current vaccines, and response to vaccines in general is reduced in most of these patients. Therefore vaccination does not substantially alter the approach to a febrile patient. Other heavily encapsulated pathogens such as H. influenza type B and meningo coccus are much less common, but at least theoretically more of a risk in the splenectomised patient, even if vaccinated. Other types of pathogens such as malaria can also be overwhelming in the absence of a spleen. The basic evaluation is similar to that for any moderately immunocompromised patient. In addition, a particularly high index of suspicion for pneumonia and meningitis, is appropriate. Therefore, in many cases, blood cultures and chest x-rays will be indicated, and the threshold for doing a lumber puncture would be lowered.

Answered by:

Dr. Michael Libman

Severe Medication Allergies and Risk of Anaphylaxis

11. Other than avoidance how ought we to handle patients with severe or potentially severe allergies to medications (e.g., penicillin, hives) and how can this be tested to determine risk of anaphylaxis?

Question submitted by:
Dr. Judy Patterson
Edmonton, Alberta

Adverse reactions to medications may be either IgE-mediated (e.g. urticaria, angioedema, upper or lower airway, GI or cardiovascular involvement) or non-IgE-mediated. Non-IgE mediated reactions may include maculopapular eruptions, drug fever, Stevens Johnson Syndrome or toxic epidermal necrolysis. Confirmatory testing may involve prick or intra-dermal skin tests (for suspected IgE-mediated reactions) or patch tests for non-IgE-mediated reactions. Adverse reactions may be due to the parent drug (e.g. penicillin) or due to a metabolite of the parent drug (i.e, the major metabolite of penicillin, benzoyl-penicilloyl-polylysine or a mixture of the minor metabolites, known as the minor determinant mix). For penicillin testing, the parent drug and metabolites are available for skin testing, and a negative skin test is 98% reliable. For other drugs, only the parent drug is available, and the resulting skin tests may be falsely negative. Patch tests, when positive are helpful in implicating a drug as a cause of a reaction, but patch tests are frequently falsely negative. Where the history or confirmatory tests clearly point to a medication as the cause of a reaction, that medication and its derivatives should be avoided. For IgE-mediated reactions, drug desensitization may be an option when performed in a monitored setting.

Answered by:

Dr. Peter Vadas

Effectiveness of Angioplasty in the Prevention of Strokes

12. How effective is angioplasty carotid ateries in the prevention of strokes?

Question submitted by:
Dr. Norman Chychota
Edmonton, Alberta

The risk of ipsilateral stroke in patients with symptomatic carotid stenosis is dependent on the degree of the arterial narrowing. Patients in whom the degree of stenosis is more that 70% should have urgent treatment, which in most individuals is carotid endartectomy (CEA). In recent years, there has been increasing interest in treating such lesions with angioplasty and stenting. These non-surgical treatment options were initially reserved for patients who were at a high risk for surgical complications. In recent years, several prospective and randomized studies have compared CEA to angioplasty and stenting. In all such studies, the risk of immediate vascular complications and long-term recurrent vascular disease was lower in patients treated with CEA. The largest study, Carotid Revacularicate Endaterectomy vs. Stenting Trials (CREST), funded by the National Institute of Health (NIH) is almost near completion and should provide important results that will help in stratification of the appropriate patients for CEA versus stenting. Until the results are known it is best that patients with symptomatic carotid stenosis are treated with CEA unless they are deemed at high risk for complications from the procedure.

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Answered by:

Dr. Ashfaq Shuaib