1. The use of valproic acid

Does the use of valproic acid for chronic nerve pain, migraine prevention, or mood disorders require ongoing blood monitoring, and, if so, what tests are essential?

Submitted by:
James Krahn, MD CCFP
Winnipeg, Manitoba

This month's topics:

Valproic acid (VA) or valproate may rarely result in some idiosyncratic adverse effects, particularly ones that are hepatic and hematologic. One of these adverse effects is the very rare, but potentially fatal hepatotoxicity. Hepatotoxicity is reported to occur in 29 of 1 million people taking valproic acid in the U.S. The greatest risk occurs in children under age two being given VA in polytherapy. Under age two, VA must be used with extreme caution, preferably in monotherapy. Minor elevations of transaminases and lactate dehydrogenase are frequent and appear to be dose related.

Rare hematologic effects, including thrombocytopenia, inhibition of platelet aggregation, leukopenia, red cell aplasia, and even more rarely, aplastic anemia have been reported. Prior to planned surgery, complete blood cell count (CBC), platelet count, international normalized ratio (INR), partial thromboplastin time (PTT), and bleeding time should be considered, particularly in someone with easy bleeding or bruising.

Prior to starting VA, baseline liver function tests, CBC, platelet count, INR, and PTT would be advisable, with repeat on one or two occasions within the first six months. If abnormal values develop post-treatment, more frequent testing may be needed. It is more important to monitor clinically for jaundice, anorexia, bleeding, or bruising.

Other rare idiosyncratic adverse events which may be related to VA include, encephalopathy from elevated blood ammonia levels and acute pancreatitis.

Answered by:
K.J. Ho, MD, FRCPC
Staff respirologist
Royal Columbian Hospital
New Westminster, British Columbia

2. Are doctors immune to certain illnesses?

While doctors are exposed daily to many patients with infectious viral diseases, we do not seem to become ill as often as one would predict. Is this due to hygiene or is it immunity acquired from repeated contact?

Submitted by:
Robert Dickson, MD, PhD, CCFP
McMaster University
Hamilton, Ontario

To some extent, both hygiene and immunity are probably involved. The role of hygiene has been demonstrated fairly well for varicella. We know that when a child acquires varicella, the attack rate among non-immune household contacts is close to 95%. Obviously, this is a highly contagious disease. However, when non-immune health-care workers (nurses in particular) are unknowingly exposed to a case of varicella in the hospital, only about 5% become infected. This suggests that the usual types of contact between health-care workers and patients is not sufficient to transmit disease in this case.

It is difficult to define the most important difference between household and "medical" contact. It is probably a combination of the intimacy of the contact, handwashing, glove use for contact with mucus membranes, and other factors.

It seems likely that immunity also plays a role. Protective immunity does develop to many, but not all, viral strains that cause upper respiratory infections. Children entering school from daycare (where there is heavy exposure to various infections) have fewer infections than those entering from home. However, since there are so many viral species and subtypes causing human infection, there will always be a certain baseline infection rate as new viruses enter the community.

Answered by:
Michael Libman, MD, FRCPC
Assistant professor
McGill University
Montreal, Quebec

3. How far-reaching is the influenza vaccine?

Does the influenza vaccine given annually protect against viruses not specifically in the vaccine, but which circulate during the winter?

Submitted by:
Robert Dickson, MD, PhD, CCFP
McMaster University
Hamilton, Ontario

The influenza vaccine contains predominantly the purified hemagglutinin and neuraminidase antigens which reside on the surface of all influenza viruses. These antigens are subtype-specific and only protect against similar subtypes. When the subtypes change, as a result of mutations or major genetic reassortment, the previous year's vaccine may not protect very well or not at all. Therefore, new vaccines must continually be prepared, although not necessarily every year if the epidemic strains remain the same.

It is important to remember that the influenza vaccine protects from influenza virus infection only. There is no protection afforded against other respiratory viruses, such as respiratory syncytial virus, parainfluenza virus, or adenovirus *etc*., which can mimic influenzal illness.

Answered by:
H. Grant Stiver, MD, FRCPC
Professor of medicine, division of infectious disease
University of British Columbia
Vancouver, British Columbia

4. Corticosteroid inhalers for COPD

Should corticosteroid inhalers be used as preventive therapy in chronic obstructive pulmonary disease patients?

Submitted by:
Hany Kamel, MD
St. Laurent, Quebec

Even in high doses, inhaled corticosteroids (ICS) cannot alter the chronic obstructive pulmonary disease (COPD) process. Only about 10% of COPD patients seem to respond to ICS with improved symptoms and these individuals likely have both asthma and COPD. An asthma component should be suspected in those COPD patients with significant allergies, heightened airway hyper-responsiveness, and those whose symptoms or lung function improve dramatically with a short-acting ß2-adrenergic bronchodilator. An oral steroid trial is not predictive of a beneficial response to ICS.

For typical, non-asthmatic COPD patients, only those with advanced COPD (forced expiratory volume in one second [FEV_1] < 50% predicted) and frequent exacerbations are likely to benefit from ICS, as high-dose ICS may reduce the frequency of COPD flare-ups by about 25%.

In the typical primary care setting, < 20% of symptomatic smokers have an FEV_1 < 50% predicted, which means most COPD patients are unlikely to benefit from ICS. This is important, because current data show increased skin fragility, bruising, thrush, and possibly an increased prevalence of cataracts associated with ICS. In addition, COPD patients are often elderly and there is data that bone mineral density decreases in patients on moderate- to high-dose ICS, although whether this is associated with an increased incidence of fractures is controversial.

Answered by:
Rick Hodder, MSc, FRCPC
Professor, divisions of pulmonary and critical care medicine
University of Ottawa
Ottawa, Ontario

5. Congested eustachian tubes

I have a young adult patient with congested eustachian tubes and no definitive allergies on testing. The patient does not respond to antihistamines or Nasonex® drops. He has pressure symptoms in the ears relieved by swallowing. Do you have any suggestions for conservative treatment measures?

Submitted by:
Irene D'Souza, MD
Willowdale, Ontario

The young adult patient described with the pressure symptoms that are relieved by swallowing is likely to have eustachian tube dysfunction (ETD). He should have a proper ear, nose, and throat evaluation and eustachian tube function evaluation, or at least a tympanometry.

Eustachian type dysfunction is affected by endogenous and exogenous conditions, such as cleft palate, respiratory allergy, or upper respiratory infections.

Drugs such as nasal steroids, antihistamines, and oral and topical decongestants have, at best, an equivocal effect on ETD. Some mechanical devices may provide temporary relief, but their value is unproven.

Patulous eustachian tube is another type of eustachian tube condition in which the patient complains of fullness or blockage and complains of hearing his own voice and breath in the ear (autophony).

Answered by:
Jaime Del Carpio, MD, FRCPC
Associate profressor, department of medicine
McGill University
Montreal, Quebec

6. Recognizing bipolar illness

What are the key factors in the recognition of bipolar illness?

Submitted by:
Gerasimos Kambites, MD, FRCPC
Ottawa, Ontario

Bipolar I disorder is characterized by one or more manic or mixed episodes, usually accompanied by major depressive episodes. This is in contrast to bipolar II disorder, which is characterized by one or more major depressive episodes accompanied by at least one hypomanic episode.

Manic episodes are, in general, relatively easy to diagnose; they are associated with elevated, expansive, or irritable mood, as well as with feelings of grandiosity, decreased need for sleep, accelerated speech and thoughts, and an increase in goal-directed activities, particularly those that may have a high potential for painful consequences.

More than a third of patients with bipolar disorder who see a mental health professional after their first manic/hypomanic episode are, in fact, misdiagnosed with unipolar depression. A similar proportion of patients fail to seek treatment for at least 10 years after the first episode.

There is a high comorbidity with anxiety disorders, particularly panic disorder, as well as substance abuse disorders, attention deficit-hyperactivity disorder, and borderline personality disorder. Unfortunately, the presence of comorbidity is associated with an overall poor outcome (*i.e.*, more frequent episodes and diminished response to medications). Dx

Answered by:
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