Consultant's Corner

Practical Answers To Your Everyday Questions

1. Elevated Vitamin B12 Level in an Otherwise Healthy Patient

High B12 level in a patient who does not take supplements. Any significance? Any further tests?

Question submitted by:
Dr. Schlanger
Toronto, Ontario

An elevated vitamin B12 level in an otherwise healthy patient with no abnormalities on the complete blood count is of no clinical significance.

Recently, serum vitamin B12 levels have been studied to determine adverse outcomes in various predictive models in inpatient populations. It may be an independent predictor of morbidity and mortality in elderly hospitalized patients and critically ill inpatients. The underlying pathophysiology for adverse outcomes, if any, has yet to be elucidated.

Also, an elevated vitamin B12 level may be present in patients with myeloproliferative neoplasms (previously called myeloproliferative disorders) such as polycythemia vera. Previous diagnostic criteria for polycythemia vera included an elevated vitamin B12 level as one of its minor criteria. It was presumed that an increase in myeloid lineage cells led to an increase in transcobalamin I and III. Vitamin B12 is bound to transcobalamins I, II, and III. Only vitamin B12 bound to transcobalamin II is physiologically important for cellular function, and this represents a small amount, about 25% of the total vitamin B12. However, it is important to recall that these patients will present with other abnormalities on history or physical (post bath pruritus, splenomegaly) and in the laboratory tests (elevated hemoglobin, hematocrit, neutrophil, or platelets).

Answered by:
Dr. Cyrus Hsia and
Dr. Kang Howson-Jan

2. Side-effects of Atypical Antipsychotic Use in Patients

A young man in his mid 20s with schizophrenia is put on olanzapine and gains 150 lbs. He displays normoglycemia and elevated total cholesterol, and LDL-C. His psychiatrist insists that I monitor this. Are there specific guidelines that can be trusted?

Question submitted by:
Dr. Layne Woodburn
Victoria, British Columbia

The use of atypical antipsychotics is associated with various metabolic abnormalities including obesity, dyslipidemia and an increase in the risk of developing diabetes. A few case reports of these agents precipitating diabetic ketoacidosis have also been published. It is recommended that doctors monitor patients for these conditions after the initiation of atypical antipsychotic agents and periodically thereafter. Therapeutic lifestyle changes, such as diet and excerise, should be encouraged.

Consideration should be given to switching to other psychotropic agents if possible, in case significant metabolic abnormailities occur. There have been some studies evaluating the role of metformin given prophylactically to these patients, but the results have been inconclusive thus far.

Answered by:
Dr. Hasnain Khandwala

Prescribing for Adult ADHD

3. For treatment of ADHD in adults do you tend to prescribe amphetamine and dextroamphetamine and save methylephenide (oral) for kids/adolescents? What is the efficacy of methylephenide (oral) in adult ADHD treatment?

Question submitted by:
Dr. Heather Sylvester
Stratford, Ontario

After comprehensive assessment and diagnosis of adult ADHD, the first-line treatment for adult ADHD is a long-acting formulation of methylphenidate or other stimulant medications.[1,2] The non-stimulant atomoxetine is often considered to be the second-line treatment.[2] There is no evidence in the literature to suggest that amphetamine and dextroamphetamine should be used as first-line treatment in adults or that osmotic-release oral system (OROS) methylphenidate should be reserved for children and adolescents. In fact, OROS methylphenidate has been approved for treatment of adult ADHD in Canada.[3]

The osmotic-release oral system (OROS) formulation of methylphenidate delivers this medication in a controlled manner over a period of 12 hours. This allows symptoms of ADHD to be controlled over the course of the day and evening. A review of the literature in one study identified four randomized controlled trials, two open label studies, and one chart review that examined the efficacy of OROS methylphenidate in adult ADHD. All clinical studies found daily dosing of OROS methylphenidate to be efficacious for treating core ADHD symptoms when compared to either placebo or immediate release methylphenidate given three times a day.[3]

Stimulants are by far the best-studied agents and have been found to be the most effective treatment for ADHD (effective in approximately 70% of patients). However, there is still some reluctance to use stimulants in both children and adults, due to concerns regarding subsequent stimulant addiction. This belief persists even though clinical studies and experience do not support this perception. As such, the stimulant medications are still the preferred agents for treatment of adult ADHD.[1]

If the patient has a personal history of substance abuse, an agent with the least potential to be abused should be utilized. Options in this case would include OROS methylphenidate or lisdexamfetamine. OROS methylphenidate is difficult to abuse given its unique formulation and lisdexamfetamine is a prodrug requiring conversion to the active medication in the blood. Alternatively, a nonstimulant (atomoxetine) could also be used.

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

Chronic Perforated Eardrum

4.

A patient has a chronic perforated eardrum and intermittent thick white/yellow discharge. He is not interested in surgery. Is there any medication that would decrease discharge?

Question submitted by:
Dr. Mihiri Wanigaratne
Edmonton, Alberta

Initially, if the infection is acute, the treatment involves careful cleaning of the ear, culture of the discharge, antibiotics, and eardrops. Blocking of the ear while showering, bathing and swimming to prevent further infection should be advised. However the sequelae and complications of chronic otitis (as we have in this case) should be clearly explained to the patient.

A patient with a perforated tympanic membrane can develop chronic otitis media. This is defined as a chronic ear infection with drainage out of the ear canal (otorrhea). The long-standing infection slowly erodes the middle ear ossicles, causing ossicular chain discontinuity. Occasionally, the infection can spread to:

- The inner ear, causing permanent sensorineural hearing loss
- To the facial nerve, causing facial nerve paralysis, or to
- The brain causing meningitis or a brain abscess

Chronic otitis media can also lead to a cholesteatoma. A cholesteatoma is a skin growth that occurs behind the eardrum. It is usually caused by repeated ear infections associated with chronic otitis media and/or cholesteatoma, which are serious conditions that require prompt treatment.

The patient should be referred to an otolaryngologist, who will assess his condition and request an audiogram and often a computed tomography (CT scan) of the temporal bones to define the extent of the disease. In general, the treatment is surgical (tympanoplasty/mastoidectomy). The use of local antibiotic prescriptions alone will not eradicate a similar condition.

Answered by:
Dr. Ted Tewfik

Performing Endometrial Biopsy in Mid-late 40s Female Patients

5.

When should we consider endometrial biopsy in a female with irregular bleeding/menses in mid-late 40s (peri-menopausal)?

Question submitted by:
Dr. Mala Dave
Burnaby, British Columbia

An endometrial biopsy should be considered for any woman presenting with irregular bleeding or menses in the mid to late 40s. Inter-menstrual bleeding or prolonged heavy bleeding in perimenopausal and anovulatory premenopausal women should be investigated. Up to 25% of all endometrial cancer cases are diagnosed in pre and perimenopausal women, thus it is critical to exclude a malignant process or identify premalignant endometrial hyperplasia with atypia before initiating treatment for bleeding complaints.

Answered by:
Dr. Cathy Popadiuk

Clinical Presentations and Lab Testing for Syphilis

6.

Please update us regarding clinical presentations and lab testing for syphilis. Has it been on the rise in our area?

Question submitted by:
Dr. L. Seaman
Inuvik, Northwest Territories

Syphilis has been on the rise for a few years now in many areas, although I cannot comment on the situation in the NWT specifically. Nevertheless, it would be wise for all clinicians to be alert for cases, particularly since this infection was close to being eradicated in Canada some years ago. The current increase is largely linked to unsafe sexual practices of men having intercourse with other men in urban regions of the country, but obviously there are no limits to where it can spread.[1] Throughout the centuries, syphilis has been a difficult diagnosis, due to its protean manifestations, including the complete absence of symptoms. Clinicians must always be watchful for unusual rashes, adenopathy, or neurological symptoms. Lab testing has recently changed. The usual protocol involved screening with a non-treponemal test, such as the Venereal Disease Research Laboratory (VDRL) or Rapid Plasma Reagin (RPR). Positives were then confirmed by a treponemal test, usually treponema pallidium particle agglutination (TPPA) or fluorescent treponemal antibody treponema pallidium (FTA-TP). The nontreponemal tests are fairly sensitive,but have many false positives (thus, requiring confirmation). They also tend to revert to negative after treatment. More recently, for reasons of lab efficiency, some labs now screen with a treponemal test. These tend to be quite sensitive and specific but also remain positive for life despite treatment. With this new testing sequence, we now often find patients with positive treponemal tests and negative (or borderline) nontreponemal tests. This may represent very early infection, remote treated infection, false positives, or even remote untreated infection. Interpretation of these results may require the help of a specialist.

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Answered by:
Dr. Michael Libman

When to Use Cholestyramine Resin for Gastroenteritis

7. When is recommending use of cholestyramine resin for gastroenteritis appropriate?

Question submitted by:
Dr. Kelly Chew
Victoria, British Columbia

Cholestyramine is a bile acid sequestering resin with a number of potential applications, including adjunctive management of dyslipidemia, serum bile acid induced pruritus, as well as choleretic diarrhea. With respect to the latter, documentation of enteric bile acid malabsorption is ideally facilitated by abnormalities in objective testing, such as with selenium homocholic acid taurine (SeHCAT). Nonetheless, the empiric use of the resin in patients with undifferentiated chronic diarrhea with plausible physiological mechanisms of bile acid cycling abnormalities is quite reasonable given the limited access to such testing. However, the role of cholestyramine in management of acute diarrhea related to gastroenteritis is unclear. Although transient bile acid malabsorption may occur as a result of gastroenteritis, the efficacy of its usage in managing diarrhea related to the acute infection has not been clearly established by the existing literature, though some data suggests that chronic diarrhea precipitated by acute gastroenteritis may be related to bile acid malabsorption responsive to cholestyramine treatment.[1,2] As such, given the typically self-limited nature of acute infectious gastroenteritis, combined with potential adverse effects and inherent challenges in administration (including binding to other concomitant medications), empiric treatment with this resin cannot be recommended.

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Answered by:
Dr. Ted Xenodemetropoulos

Risks in Young Children Taking Omega/DHA Tablets or Oils?

8.

Are there any risks in young children taking omega/DHA tablets or oils?

Question submitted by:
Dr. Patricia Menard
Antigonish, Nova Scotia

The administration of omega-3 fatty acids to children is now fairly common, notably as many infant formulas are now omega-3 supplemented. It has been demonstrated in several studies that supplemental DHA and omega-3 may confer neurodevelopmental benefits, notably among infants whose diet is deficient in DHA. Although the use of fish oil and omega-3 supplements appears to be very safe, the U.S. FDA has recommended that eicosapentaenoic acid or DHA supplements for adults should not exceed 3 gm/day in adults, and it would be reasonable to consider these limits on an age-adjusted basis for young children. It should also be noted that young children are usually unable to take tablets or capsules on a regular basis and that the average medication naïve child cannot take tablets until age seven or eight.

Answered by:
Dr. Michael Rieder

Interactions of Natural Medicines with Psychotropic Medications

9. What natural medicine is known to interact with psychotropic medications (antidepressants, antipsychotics, mood stabilizers, *etc.*)?

Question submitted by:
anonymous

Natural medicines are increasing in popularity, because many patients believe they are healthier and safer than conventional medicines. However, despite their natural components, these agents can still be associated with serious drug interactions and side effects. In a patient population taking antidepressants, antipsychotics, or mood stabilizers, this poses a challenge to physicians, because several natural medicines affect the same neurotransmitters that traditional agents have an impact on at the neuronal synapse (*e.g.,* serotonin, dopamine, norepinephrine).

Tryptophan and melatonin are two examples of natural medications whose effects on neurotransmitters may be an important consideration when combined with traditional psychiatric medications, as sleep disorders are commonly associated with psychiatric conditions, such as depression and bipolar disorder.[1,2] Tryptophan has been indicated in the treatment of sleep disorders, because it acts as a precursor molecule for melatonin, a neurohormone that is responsible for regulating sleep cycles.[3] Tryptophan also acts as an immediate metabolic precursor of the neurotransmitter serotonin, which regulates mood and emotion.[2] The subsequent conversion of tryptophan to serotonin is what causes concern regarding the concomitant use of this supplement with antidepressants, antipsychotics, and mood stabilizers that also have serotonergic properties, because the concurrent use of such medications may significantly increase the level of serotonin in the synapse. As a result, a pharmacodynamic interaction, known as serotonin syndrome, which is characterized by neuromuscular, cognitive, and autonomic changes, can occur.[4,5,7]

Similar safety concerns result from the potential for increased serotonin levels and development of serotonin syndrome, primarily of the reuptake of serotonin from the neuronal synapses through the use of another popular natural medicine, the herb: St. John's Wort (frequently used to treat depression secondary to its inhibition). This potential interaction is of particular concern in patients who are on a selective serotonin reuptake inhibitor (SSRI) and St. John's Wort, also a potent inhibitor of CYP3A4.[6,7]

When considering the safety of specific natural medicines, it is important to determine whether the way the natural product is metabolized is known. If its metabolism involves any of the cytochrome P450 enzymes, it is important to consider if the patient is on any antidepressants, antipsychotics, or mood stabilizers that are also substrates, inhibitors, or inducers of the same cytochrome P450 enzymes and how this might impact the resultant levels of the natural or traditional medicine or prescribed agent. In summary, before suggesting the use of natural medicines, clinicians should determine if they could potentially effect any of the neurotransmitters associated with traditional agents, as well as consider whether any potential drug interactions mediated by the cytochrome P450 enzymes exists.

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

Testing a Patient's Immunity to Tetanus, Measles, and Mumps

10.

How would you test one's immunity to tetanus, measles and mumps?

Question submitted by:
Dr. Anwar Asady
Mississauga, Ontario

There are a few specialty labs that are capable of measuring antibodies against these infections, and interpretive criteria exists for assessing whether a given antibody titre is suggestive of immunity. However, it is often not worthwhile ordering these tests. The first problem is that the interpretive criteria is not well validated clinically. The second problem is that sending these tests out to special labs means the turnaround time will probably be quite long. So I would recommend that if you cannot document that the patient has followed the proper vaccination schedule, or that he/she is likely immune due to previous infection, the practitioner should simply vaccinate the patient by supplying any missing doses. This has the great advantages of providing immediate protection, and not risking a loss to follow up while awaiting results. There is no harm in giving doses that might be unnecessary, other than the small cost. It used to be said that giving a tetanus booster dose at less than a five year interval could cause increased pain at the injection site, but recent studies suggest this is not true. And if you give MMR (a live vaccine) to a person who is actually immune, they will simply rapidly kill off the vaccine virus, and thus rarely have the mild febrile illness that may follow primary vaccination.

Answered by:
Dr. Michael Libman