1. Iron Supplementation in Thalassemia Minor

I have a few patients with both thalassemia minor and low ferritin levels. Should these patients be treated with iron supplements, or should they be avoided for fear of iron overload?

Submitted by: Loredana Di Santo, MD, Maple, Ontario

The thalassemias are a group of heterogenous inherited disorders of globin chain synthesis. The normal adult hemoglobin (HbA) is composed of two α and two ß chains. Various mutations in the α– or ß-globin genes lead to different α– or ß-thalassemias, respectively. Iron depletion (low iron stores) is common, particularly in populations such as infants and pregnant women. Inappropriate iron supplementation should be avoided in the majority of patients with asymptomatic thalassemia minor.

ß-thalassemia trait (or thalassemia minor) results from a mutation in one of the ß-genes, one on each chromosome 16. This is usually identified with an increase in HbA2, which is composed of two α and two ∂ chains. Typically, these patients are asymptomatic. Concurrent iron depletion may lower the HbA2 level and delay the diagnosis. It is essential to rule out concurrent iron depletion and avoid inappropriate exogenous iron supplementation. However, in certain patients with both iron depletion and ß-thalassemia, such as pregnant women, iron supplementation has been advised.

α–thalassemia results from gene mutations that lead to quantitative reductions in α–globin. Unlike the ß-genes, there are a total of four α–genes; there are two on each of the chromosome 11s. Usually, a mutation in only one of these genes will result in a silent carrier state. The silent carrier state has no consistent hematologic manifestations; often the individual is asymptomatic and does not have microcytosis. With concurrent iron deficiency, microcytosis is present and replacing iron is similar to that of the general public. However, mutations in two of the α-genes lead to the α-thalassemia trait. These individuals may have a similar clinical presentation to someone with ß-thalassemia trait. Hemoglobin electrophoresis alone typically is not sufficient for diagnosis, and often gene sequencing for the most common varieties is required. Iron depletion in a patient with α-thalassemia trait is similar to the previous discussion for ß-thalassemia trait.

Answered by: Dr. Cyrus Hsia and Dr. Leonard Minuk

2. Narrowband Vs. Standard UVB

Can you comment on the advantage of narrowband UVB over standard UVB?

Submitted by: Bernard Séguin, MD, Ottawa, Ontario

Broadband UVB (bUVB) uses wavelengths ranging from 280 to 320 nm to treat various dermatoses, especially psoriasis vulgaris. Erythema (sunburn) is primarily caused by lower wavelengths (*i.e.*, less than 305 nm). The most therapeutic wavelengths for psoriasis are known to be between 296 and 313 nm. Therefore, narrowband UVB (nUVB) bulbs were developed that primarily emit 311 nm wavelengths. The theory was that nUVB would maximize the efficacy against psoriasis while minimizing the risk of sunburn, which would limit bUVB therapy. This theory has been shown to be valid, and is the major advantage of nUVB.

nUVB has also demonstrated efficacy in treating vitiligo and atopic dermatitis. Several clinical trials in psoriasis treatment have shown it to be more effective than bUVB, although the difference in treatment response was small. The relative risk of nUVB compared to bUVB remains uncertain, as follow-up studies of nUVB are of short duration.

Answered by: Dr. Richard Haber

3. Antipsychotics to Treat BPD-Related Insomnia

Are antipsychotics useful for the treatment of insomnia in patients with borderline personality disorder?

Submitted by: Marie-Andrée Beauchemin, MD, Terrebonne, Quebec

Patients with borderline personality disorder are known to experience severe, unpredictable mood swings with intense labile affect. When these mood swings include strong urges to self-harm, often associated with psychic agitation and intense anger, as frequently seen in borderline patients, then prescribing an atypical antipsychotic medication such as olanzapine or Seroquel is indicated for management of the borderline patient. If an underlying depressed mood is suspected, then adding an antidepressant is recommended.

If the insomnia is due to intense negative affect, including recurrent angry ruminations that are not justified or called for, then prescribing an antipsychotic is appropriate. Otherwise, the insomnia should be managed with sleeping medications such as Imovane 5 to 7.5 mg q.h.s. p.o., or a sedating antidepressant such as trazodone 50 to 100 mg q.h.s. p.o.

Answered by: Dr. Hany Bissada

4. Treating Elevated TSH

What is the treatment of elevated TSH (between 5 and 10 mU/L)?

Submitted by: J. Dawson, MD, Richmond Hill, Ontario

This is generally referred to as subclinical hypothyroidism (high TSH and normal free T4). The causes are the same as overt hypothyroidism (high TSH and low free T4). Treatment with thyroid hormone is controversial in cases of subclinical hypothyroidism. However, beginning treatment with low doses of levothyroxine (25 to 50 mcg) is recommended in the following situations:

- patients with symptoms of hypothyroidism (three to six month trial)
- presence of thyroid nodules (may reduce size and/or growth)
- pregnancy or contemplation of pregnancy (fetus does not produce thyroxine in first trimester)
- TSH consistently > 10 mU/L
- High cholesterol/LDL (may improve profile)

The important thing is to monitor the TSH in four to six weeks following treatment initiation to ensure the right dosing.

Answered by: Dr. Ally Prebtani

5. HPV Vaccine for Women Over 26-Years-of-Age

Can we prescribe the HPV vaccine for a woman older than 26-years-of-age?

Submitted by: **Antoine St. Pierre, MD,** Charny, Quebec

The current human papillomavirus (HPV) vaccine in Canada is approved for women aged 13 to 26, as this was the age group in which the studies were performed and indicated to Health Canada. The studies were done in this age group because the peak incidence of HPV infection is within five to ten years of the first sexual experience (15 to 25-years-of-age). A recent study has demonstrated that the quadrivalent HPV vaccine is efficacious in women aged 24 to 45 years, who were not yet infected with the relevant HPV types at the beginning of the study. Routine vaccination for women over 26 should not be recommended, but may be given depending on the individual circumstances. The HPV vaccine will not be paid by third party insurers unless Health Canada approves it for this age group. However, in a woman who is sexually naive or recently sexually active at the age of 26 or older, there is no reason to deny the HPV vaccine. In addition, even sexually active women may not have been exposed to the HPV strains associated with cervical cancer.

Resource

1. Muñoz N, Manalastas R, Pitisuttithum P, et al: Safety, Immunogenicity, and Efficiency of the Quadravalent Human Papillomavirus (Types 6, 11, 16, 18) Recombinant Vaccine in Women Aged 24-45 Years: A Randomized, Double-blind Trial. Lancet 2009;373(9679):1949-57.

Answered by: **Dr. Victoria Davis**

6. Plasmapheresis for Guillain-Barré Syndrome

What is the role of plasmapheresis in Guillain-Barré syndrome and does it work to improve the symptoms?

Submitted by: K. Patel, MD, Alberta

Plasmapheresis is one of the mainstays of treatment for Guillain-Barré syndrome, and is most effective if given within the first week of onset of symptoms of Guillain-Barré. Most patients require four to six treatments on alternate days. Plasmapheresis results in decreased hospitalization and mechanical ventilation time, and reduction of time for patients to walk again. It also results in more patients returning to full muscle stength in one year's time.

Resource
1. Rana AQ. 2009. Chapter 4. In: A Synopsis of Neurological Emergencies. Bloomington (IN): Authorhouse. p43-49.

Answered by: Dr. Abdul Qayyum Rana

7. Effectiveness of IV Bisphosphonates in Metastatic Cancer

How effective are IV bisphosphonates for bone pain in metastatic cancer?

Submitted by: Lorraine Wood, MD, Toronto, Ontario

Bisphosphonates inhibit osteoclast function and decrease pain in metastatic cancer to the bone by diminishing microfractures, but they also seem to have a direct anti-tumour activity that is being investigated. Bisphosphonates should be considered in cases of metastatic bone cancer not only for pain control, but also to manage hypercalcemia and decrease the likelihood of gross fracture. The magnitude of the effect on pain appears to be moderate: in one study on metastatic prostate cancer, where zoledronic acid 4 mg IV was given every three weeks for 15 months, the Brief Pain Inventory score (which ranges from 0 to 10) was 2.0 at baseline in the zoledronic acid group, and had risen by 0.58 after 18 months. In the placebo group, the score was 2.1 at baseline, and had risen by 0.95 after 18 months. The benefits were maintained at 24 months.

Resources
1. Saad F, Gleason DM, Murray R, et al: Long-term Efficacy of Zoledronic Acid for the Prevention of Skeletal Complications in Patients with Metastatic Hormone-refractory Prostate Cancer. J Natl Cancer Inst. 2004 Jun 2;96(11):879-82.
2. Costa L, Lipton A, Coleman RE: Role of Bisphosphonates for the Management of Skeletal Complications and Bone Pain from Skeletal Metastases. Support Cancer Ther. 2006 Apr 1;3(3):143-53.

Answered by: Dr. Michael Starr and Dr. Emil Nashi

8. Montelukast Use for Allergies

Please discuss montelukast use in allergic but non-asthmatic patients.

Submitted by: Laura McConnell, MD, Mississauga, Ontario

Nasal challenge studies have shown that both histamine and cysteinyl leukotrienes activate inflammation in allergic states, providing sound biochemical reasoning for the use of leukotriene inhibitors in allergic rhinitis. Montelukast (Singulair) has been found helpful in treating the upper airway symptoms of allergic rhinoconjunctivitis (AR). The degree of effectiveness is limited, and is generally thought to be similar to that achieved by use of non-sedating antihistamines, but inferior to the effectiveness of nasal corticosteroids.[1] Interestingly, concomitant use of montelukast and loratadine was not found to significantly improve daytime allergic symptom scores compared with each agent separately.[2] Although pruritis and sneezing may be effectively helped by use of antihistamines, the entire spectrum of AR symptoms, including congestion, sneezing, rhinorrhea and pruritis, are helped best with nasal corticosteroids. With regards to other non-asthmatic conditions, the evidence for use of montelukast is sparse. In a single-blind, placebo-controlled, crossover study, montelukast was shown to be an effective agent in refractory chronic idiopathic urticaria.[3] Leukotriene modifiers have been used for the treatment of eosinophilic conditions not related to asthma, such as eosinophilic esophagitis and eosinophilic gastroenteritis.[4,5]

References
1. Pullerits T, Praks L, Skoogh BE, et al: Randomized Placebo-controlled Study Comparing a Leukotriene Antagonist and a Nasal Glucocorticoid in Seasonal Allergic Rhinitis. Am J Respir Crit Care Med 1999;159(6):1814-18.
2. Meltzer E, Malmstrom K, Lu S, et al: Concomitant Montelukast and Loratadine as Treatment for Seasonal Allergic Rhinitis. J Allergy Clin Immunol 2000;105(5):917-22.
3. Erbagci Z: The Leukotriene Receptor Antagonist Montelukast in the Treatment of Chronic Idiopathic Urticaria. J Allergy Clin Immunol 2002;110(3):484-88.
4. Attwood S, Lewis C, Bronder C, et al: Eosinophilic Esophagitis: A Novel Treatment Using Montelukast. Gut 2003;52:181-85.
5. Schwartz DA, Pardi DS, Murray JA: Use of Montelukast as Steroid-sparing Agent for Recurrent Eosinophilic Gastroenteritis. Dig Dis Sci 2001;46(8):1787-90.

Answered by: Dr. Tom Gerstner

9. Eradicating Molluscum Contagiosum in Children

What is the best treatment to eradicate molluscum contagiosum in small children?

Submitted by: Angela MacArthur, MD, Calgary, Alberta

Molluscum contagiosum is caused by a human DNA pox virus that is autoinoculable. Treatment for molluscum contagiosum is not very effective, and there definitely needs to be a prophylactic vaccine or an effective antiviral agent developed in the future. Treatment is especially problematic in young children, as they do not tolerate painful therapies and multiple treatments are often necessary to clear molluscum lesions. A normal course of molluscum contagiosum in an immunocompetent patient is spontaneous resolution with time, although this can take six months, even up to five years in extreme cases. Therefore, observation is an acceptable option in young children with properly informed parents.

An updated 2009 Cochrane Review of randomized controlled trials of therapy for molluscum contagiosum concluded that no single intervention has been shown to be convincingly effective in the treatment of molluscum contagiosum.

From a practical point of view, I find the best tolerated and most effective therapy for molluscum contagiosum in young children is topical cantharidin 0.7%, which is a blistering agent derived from a species of blister beetle. This treatment is not painful when initially applied and is therefore tolerated by children, but can become painful once the blisters develop over the course of a few hours to a day. The other limiting factor is that multiple treatments are often required, need to be repeated every two to three weeks and can only be applied by the physician, not by the child's parents. Other treatments to be considered include liquid nitrogen and curettage of lesions, but neither is tolerated well by children. Topical 5% imiquimod cream applied overnight three times weekly can be prescribed as an off-label treatment, but in my experience it has not been very effective. Dx

Answered by: Dr. Richard Haber