



## Stress-Induced Cardiomyopathy

1.

### Is cardiac injury from pheochromocytoma similar to that of Takotsubo syndrome?

Question submitted by:  
**Dr. Ritchie Strachan**  
Winnipeg, Manitoba

Stress-induced cardiomyopathy, also called transient left ventricular (LV) apical ballooning, broken heart syndrome and, in Japan, takotsubo cardiomyopathy, is an increasingly reported syndrome characterized by transient apical LV dysfunction that mimics MI, but in the absence of significant coronary artery disease. Stress-induced cardiomyopathy is much more common in women than men. The onset of stress-induced cardiomyopathy is typically triggered by an acute medical illness or by intense emotional or physical stress (e.g., death of relatives, particularly if unexpected, domestic abuse, arguments, catastrophic medical diagnoses, devastating financial or gambling losses, natural disasters).

There are similarities between stress-induced cardiomyopathy and the transient LV dysfunction sometimes seen in the setting of acute brain injury, which has been postulated to be related to catecholamine excess.

While in the case of pheochromocytoma, patients typically present with concentric LV hypertrophy or myocarditis acutely with catecholamine crisis with decreased systolic function which is reversible upon treatment of pheochromocytoma.

Answered by:  
**Dr. Chi-Ming Chow**

## Children with Ingrown Toenails

2.

### What is the best treatment for an ingrown nail, for a five-year-old child who is prone to ingrown toenails?

Question submitted by:  
**Dr. Grady Hamilton**  
Toronto, Ontario

Ingrown toenails in children are usually a problem caused by cutting style (*i.e.*, how the nail is cut). Parents often cut the nail in an aggressively curved manner, which will lead to the nail at the edges growing into the flesh of the nail. When treating the ingrown toenail, frequent elevation of the edge of the nail with a soft blunt object, such as part of a tongue depressor, may be very useful and having the child soak

their foot for five or 10 minutes prior to doing this is helpful. For prevention, ensuring that the nail is cut in a squarish rather than overly curved manner is important. The edges of the nail need to grow past the skin edge. As well, avoid overly tight shoes.

Answered by:  
**Dr. Michael Rieder**

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## Magnesium Supplementation in Diabetic Patients

### 3. Is magnesium supplement a good adjunct in diabetes?

Question submitted by:

**Dr. E. J. Framzah**  
Toronto, Ontario

Magnesium is a critical co-factor in many enzymatic reactions and is essential for energy dependent transport systems, glycolysis and oxidative energy metabolism. It participates in intracellular signaling systems, insulin receptor activity and has effects on platelet aggregation and vascular smooth muscle tone. Magnesium deficiency has a negative effect on insulin signaling, insulin mediated glucose uptake, glucose induced insulin secretion, all leading to hyperglycemia. Hypomagnesemia has also been shown to be associated with a low HDL-C, increased total cholesterol, LDL-C and triglyceride levels. Small experimental studies have also demonstrated that magnesium deficiency accelerates the atherosclerotic process. The recommended dietary allowance of magnesium is between 300 mg and 400 mg q.d. Magnesium is primarily found in bran and germ. The results of magnesium supplementation on glucose metabolism

in patients with diabetes have been inconsistent. A meta-analysis of nine randomized controlled trials (RCTs) demonstrated some reduction in fasting plasma glucose and improvement in HDL-C levels, but there was no effect on long-term glycemic control. All trials were also short-term and underpowered.

Thus, though there is strong biological plausibility for the effect of magnesium on metabolic and CV risk factors, in the absence of large long-term RCTs, the recommendations of the American Diabetes Association are that there is no clear evidence of benefit from mineral supplementations in people with diabetes who do not have underlying deficiency. The best current recommendation would be to include magnesium-rich foods in the usual diet.

Answered by:

**Dr. Hasnain Khandwala**

## Long-Term Hair Colouring

### 4. Are there any side-effects with long-term hair colouring?

Question submitted by:

**Dr. Jane Purvis**  
Peterborough, Ontario

The most common side-effect is allergic contact dermatitis. Paraphenylenediamine, or PPD, is an aromatic amine—it is the frequent agent triggering the allergic reactions. There is an ongoing debate whether there is an increased risk of leukemia or lymphoma with long-term colouring, but any possible effect in this

regard is small and difficult to measure. There is some suggestion that newer hair dye preparations (since 1980) may be safer in terms of carcinogenic risk.

Answered by:

**Dr. Scott Murray**

## 5.

## Foods That Affect Vision

**What kind of food will affect eye vision?**

Question submitted by:

**Dr. David Yu**

*Scarborough, Ontario*

We are indeed fortunate in North America that we can ask this kind of question. In the Third World, it is more what kind of nutritional deficiency can have profoundly damaging effects on vision. The epidemic of age-related macular disease has led many to search for nutritional answers for this and other sight-threatening conditions. The classic story about food and vision relates to Royal Air Force fighter pilots during the early part of World War II. The British were using a primitive radar to detect incoming enemy planes and the Germans were surprised at how quickly the fighters were able to respond to the threat. The story was put out that the fighter pilots were eating vast quantities of carrots, thus enhancing their night vision. Like all the best hoaxes, there is a grain of potential scientific truth in that carrots contain  $\beta$ -carotene which is molecularly similar to visual purple.

The Age-Related Eye Disease Study (AREDS) looked at the effects of vitamin C, vitamin E,  $\beta$ -carotene, zinc and copper on the progression of 3,600 patients with varying stages of age-related macular disease. The surprising result was that the progression from dry to wet disease was reduced by 25% in those patients taking the Areds formulation. Subsequently, it was found that lutein and zeaxanthin might also be beneficial and either or both of these was added to most Areds formulas.

The Areds II trial is now underway and this is looking at the addition of the macular xanthophylls (lutein and zeaxanthin) and/or long chain omega-3 fatty acids (docosahexaenoic acid and eicosapentaenoic acid) on the progression to advanced age-related macular degeneration.

Lutein and zeaxanthin are members of a group of phytochemicals found in fruits and vegetables. Lutein is found in green vegetables, particularly spinach and egg yolks appear to facilitate the bio-availability of lutein. The combination of a hard-boiled egg and a spinach salad would, therefore, seem to be ideal. Spinach also contains a host of other potentially beneficial substances, including omega-3 fatty acids, but these are found in greatest concentration in fish. The visual benefits of blueberry, bilberry, Eyebright and other herbs are widely touted but there is little supporting scientific evidence.

The take home message here is that of all the foods for which ocular benefits are claimed, spinach is the undoubted king. Popeye was obviously much smarter than any of us realized.

Answered by:

**Dr. Malcolm Banks**



## Causes and Treatment of Anal Fissures

6.

### Can you revisit all the causes of anal fissures and all the available treatment options?

Question submitted by:  
**Dr. Mario B. Boutin**  
*Laval, Quebec*

An anal fissure is a superficial linear tear in the squamous epithelium at or just inside the anal verge. A sentinel skin tag just distal to the fissure may be seen. Most anal fissures occur in the midline, usually posteriorly. If they occur off the midline other conditions, such as Crohn's disease, ulcerative colitis, HIV/AIDS, TB, syphilis, leukemia, or cancer must be considered. Sigmoidoscopy can be traumatic to the patient and usually reveals minimal diagnostic information. Examination under anesthesia is sometimes warranted.

The goals of therapy consist of relaxation of the internal sphincter, passage of soft stool and pain relief. Initial therapy consists of increased dietary fiber to keep the stools soft and formed and warm sitz baths following bowel

movements to relax the sphincter. Topical anesthetic and steroid creams and suppositories to soothe the fissure are often prescribed. Multiple trials have shown that 0.2% or 0.4% nitroglycerin ointment can be effective at relaxing the internal sphincter. Topical nifedipine and oral diltiazem ointment have also been shown to be effective. If these fail, Botox into the internal anal sphincter may be successful. A surgical procedure, such as a lateral internal sphincterotomy could be considered when medical therapy fails. Medical therapy is successful in the majority of patients, with surgery being reserved for refractory cases.

Answered by:  
**Dr. Jerry McGrath**

## Bone Pain with Use of Filgrastim

7.

### Does filgrastim cause bone pain? If so, what is the mechanism?

Question submitted by:  
**Dr. Maury O'Neil**  
*Collingwood, Ontario*

Filgrastim is usually associated with bone pain (in about 25% of patients), mainly aching, in cancer patients who usually receive it for up to seven consecutive days. The mechanism has never been elucidated, but in most reported cases, it occurs at sites of bone marrow generation. Patients receiving chronic filgrastim for

"benign" severe neutropenia are said to experience bone pain early and presumably have less severe symptoms later. This observation may provide some clues as to the cause.

Answered by:  
**Dr. Kang Howson-Jan and Dr. Kamilia Rizkalla**

8.

## Vaccines for Patients Taking Biologic Agents

### Which vaccines are permitted for patients taking biologics for arthritis?

Question submitted by:

**Dr. Kathleen Davis**  
Ottawa, Ontario

The prevention of infection is especially important for patients taking biologic agents for arthritis. Children should be up-to-date with all of their vaccines prior to starting therapy. Live vaccines, such as varicella and the Measles, Mumps and Rubella vaccine are contraindicated. The influenza vaccine should be given to this group of patients even if they are not in a traditional high-risk group, as they are at increased risk for pulmonary infections. The new vaccines against HPV should also be considered in appropriate candidates, as it has been shown that patients with some inflammatory diseases have a higher rate of abnormal Pap tests.

Patients with active rheumatoid arthritis, including those on biologic agents, have been shown to have a decreased response to vaccinations. However, the response is adequate to continue to recommend routine vaccination. Vaccination has not been shown to cause arthritis flares in patients with stable disease.

Answered by:

**Dr. Elizabeth Hazel**

Pennsaid® is indicated for the treatment of symptoms associated with osteoarthritis of the knee(s) only, and of not more than three months duration, whether continuous

Serious GI toxicity, perforation or GI time in patients diclofenac sodium. In not been associated

Renal toxicity has been seen in patients taking NSAIDs, and those with impaired renal function, heart failure, liver dysfunction, the elderly are at greatest risk. In clinical studies with Pennsaid®, no increase in other renal toxicity has

Pennsaid® is contraindicated in patients with active peptic ulcer, a history of recurrent ulceration or active inflammatory GI disease, impairment, active liver disease or deteriorating kidney function. Pennsaid® is contraindicated in patients with hypersensitivity to diclofenac, dimethyl sulfoxide, propylene glycol, glycerine, alcohol or to other ASA/NSAID products. The potential for cross-reactivity with other NSAIDs must be borne in mind. Pennsaid® is contraindicated in patients with complete or partial ASA intolerance syndrome: fatal anaphylactoid reactions have occurred in such individuals.

Pennsaid® should be given under close medical supervision to patients with a history of ulcer or inflammatory disease of the GI tract, such as ulcerative colitis or Crohn's disease.

Commonly reported application site side effects, Pennsaid® (vs. placebo) were: dry skin, 41.9% (6.9%); rash, 9.6% (2.9%); and paresthesia, 7.9% (10.3%).

For full information, please see Pennsaid® Product Monograph.

for the treatment of with osteoarthritis of for a treatment regimen three months duration, or intermittent.

such as peptic ulceration, bleeding can occur at any treated with NSAIDs, including clinical studies, Pennsaid® has with serious GI toxicity.

been seen in patients taking impaired renal function, heart those taking diuretics, and risk. In clinical studies with urea or creatinine, or any been observed.

in patients with active recurrent ulceration or active significant hepatic or renal disease or deteriorating Pennsaid® is contraindicated with hypersensitivity to diclofenac, dimethyl sulfoxide, propylene glycol, glycerine, alcohol or to other ASA/NSAID products. The potential for cross-reactivity with other NSAIDs must be borne in mind. Pennsaid® is contraindicated in patients with complete or partial ASA intolerance syndrome: fatal anaphylactoid reactions have occurred in such individuals.

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## Omega-3 Supplements and Allergies

9.

### Can patients allergic to fish and seafood take omega-3 supplements? Is there a risk of allergy?

Question submitted by:  
**Anonymous**

Allergies to fish and shellfish are among the eight most common food allergies in the North American population. Allergic reactions to fish and shellfish, along with reactions to peanuts and tree nuts, are responsible for most life-threatening and fatal reactions to foods. Fish and shellfish allergies are often lifelong.

Omega-3 fatty acids are a family of polyunsaturated fatty acids derived from fish that have been shown in large clinical trials to reduce the incidence of CV disease. Research has shown that they decrease risk of arrhythmias, decrease triglyceride levels, decrease growth of atherosclerotic plaque and have a modest effect on lowering BP. Omega-3 fatty acid supplements have been shown to afford protection from cyclosporine toxicity

in organ transplant recipients and reduce morning stiffness and joint tenderness in patients with rheumatoid arthritis.

Allergic reactions to foods are triggered by allergenic proteins in those foods. These proteins contain the IgE-binding epitopes that trigger allergic reactions. Fish protein in omega-3 fatty acid supplements can potentially trigger allergic reactions in patients with allergy to fish. Manufacturers routinely recommend that consumers or patients with fish allergy not use these supplements because of the potential for residual protein to cause allergic reactions.

Answered by:  
**Dr. Peter Vadas**

## Lactose Intolerance in Toddlers Following GI Infections

10.

### Would a toddler develop lactose intolerance after a viral GI infection (e.g., Norwalk virus)?

Question submitted by:  
**Anonymous**

The transient development of lactose intolerance following a viral GI infection is very common and to be frank, is probably overdiagnosed. While there is no question that some infants do have lactose intolerance with loose stools after viral gastroenteritis, studies done over the past decade have suggested that the majority of toddlers can tolerate milk within several days of the resolution of viral enteritis. Some

toddlers will have frequent stools for up to several weeks after a severe viral gastroenteritis, but the most effective therapy for these children is not prolonged clear fluids, but rather provision of simple calories (*i.e.*, easy to digest foods) and patience.

Answered by:  
**Dr. Michael Rieder**

11.

## Treating Hypothyroidism During Pregnancy

**At what level should we treat hypothyroidism during pregnancy and which study supports those values?**

Question submitted by:

**Dr. Annie Pepin**  
Bromont, Quebec

The requirements of thyroid hormone during pregnancy can often increase by as much as 50%. There are a number of reasons for it; the increase in estrogen-induced thyroxine-binding globulin (TBG) makes less free thyroid hormone available. There is also increased urinary iodine excretion, as well as increased deiodination of thyroid hormones due to an increase in placental deiodinase activity. These also reduce maternal thyroid hormone levels. The fetal hypothalamic pituitary thyroid axis becomes functional after about the tenth to twelfth week of gestation; before this time, it is dependent on the maternal thyroid hormone. Severe maternal hypothyroidism can lead to fetal hypothyroidism and cause fetal goiter and cretinism. Untreated maternal hypothyroidism is also associated with an increase in obstetrical complications. Thus, given the safety of thyroid hormone and the adverse maternal and fetal outcomes associated with untreated hypothyroidism, most physicians would err on the side of caution and treat, without awaiting data from randomized controlled trials (RCTs). In some respects it is analogous to treating gestational diabetes mellitus (GDM). Very little evidence existed that treating GDM has significant maternal/fetal benefits.

Furthermore, as withholding thyroid hormone supplementation in such cases would be considered unethical, I am not aware of any RCTs in this area.

Recently however, there has been increased interest in treating even mild/subclinical hypothyroidism during pregnancy (elevated TSH, normal free T4)—an entity which most physicians would not necessarily treat otherwise. Again, a prospective double-blind RCT will probably never be performed to answer the question. We have some answers from a study published about 10 years ago which linked a low IQ level in offsprings of mothers who were hypothyroid during their pregnancy. Even in mothers who were subclinically hypothyroid, the offsprings scored an average of eight points lower. However, this was a retrospective study and does not prove that treating these mothers would have had any impact on the child's IQ, but most of the evidence and push for treating even mild forms of hypothyroidism comes from this study.

Answered by:

**Dr. Hasnain Khandwala**

*Recently however, there has been increased interest in treating even mild/subclinical hypothyroidism during pregnancy.*



## Different Treatment Options for GERD

12.

**With all of the therapy out there for gastroesophageal reflux disease (GERD), is there one that stands out (irrespective of cost)? How about side-effects and safety profile, recurrence rate or complications?**

Question submitted by:

**Dr. Nathalie Leroux**  
Fenwick, Ontario

The easiest, most cost effective treatment for GERD consists of lifestyle modification. Elevation of the head in bed by six inch blocks under the legs is a proven strategy for patients with nocturnal or laryngeal symptoms. Dietary avoidance of reflux-related foods including fatty foods, chocolate, peppermint, caffeine, spearmint, citrus, spicy foods and alcohol may also alleviate symptoms. However, it is often very difficult for patients to avoid these foods. When lifestyle modification fails, I generally recommend the “step up” approach. This refers to beginning with lifestyle and dietary changes and increasing the therapeutic intervention to achieve symptom control. The next step consists of antacid use followed by OTC histamine receptor antagonists (H2 blocker). If these fail, prescription H2 blockers or a PPI are very effective treatments. PPIs are the most effective agents for healing esophagitis but also the most expensive. Prokinetic drugs, like domperidone, can be used as an adjunct in patients with persistent symptoms despite PPIs.

If medical therapy fails, surgery is an option. The various surgical approaches focus on restoring

the lower esophageal sphincter pressure. Wrapping the distal esophagus with a portion of stomach increases the pressure. This, however, can be complicated by dysphagia or the inability to belch, leading to the gas bloat syndrome. The Nissen fundoplication is the most common procedure with improvement occurring in 85% to 90% of patients.<sup>1</sup>

Novel endoscopic therapies for GERD have provided a potential alternative to medical or surgical therapies. Three of these therapies include an endoscopic sewing capsule, an endoscopic suturing device and a plicating device. The three of these devices are designed to allow endoscopic sewing from the tip of a gastro-scope. None of these treatments have been sufficiently studied to be recommended as a standard treatment option for GERD.

Reference

1. Ellis FH: The Nissen Fundoplication. *Ann Thorac Surg* 1992; 54(6):1231-5.

Answered by:

**Dr. Jerry McGrath**

*The easiest, most cost effective treatment for GERD consists of lifestyle modification.*



## Investigating Hypoglycemia

### 13. How do you investigate hypoglycemia?

Question submitted by:  
**Dr. Michele MacLean**  
Kennetcook, Nova Scotia

For the sake of discussion, I am assuming that this refers to non-diabetic patients who are not on any hypoglycemic agents. Before an extensive investigation is undertaken, it is important to confirm the presence of Whipple's triad (*i.e.*, symptoms suggestive of hypoglycemia, documentation of low serum glucose concentrations and alleviation of symptoms after the administration of glucose). A detailed medication history to rule out drug-induced hypoglycemia is essential as various drugs, such as alcohol, salicylates, quinine, pentamidine, *etc.*, can cause hypoglycemia. Renal failure and chronic liver disease, sepsis and factitious hypoglycemia caused by intentional use of insulin or oral hypoglycemic agents need to be ruled out. Various endocrinopathies, such as adrenal insufficiency,

growth hormone deficiency, insulinoma, *etc.*, need to be excluded. Further testing depends on the diagnostic suspicion and usually includes performance of a supervised 72-hour fast in the hospital and measurement of insulin, proinsulin, ketones, cortisol, *etc.*, once hypoglycemia occurs. An oral glucose tolerance test, though often ordered, should not be performed, as misleading results are obtained. I would recommend that patients with suspicion of a true hypoglycemic disorder be referred for specialized assessment.

Answered by:

**Dr. Hasnain Khandwala**

## Perioral Dermatitis

### 14. Why do antibiotics help perioral dermatitis?

Question submitted by:  
**Dr. L. Pilot**  
Saskatoon, Saskatchewan

We know that perioral dermatitis often improves with oral antibiotics, such as tetracycline, minocycline and doxycycline. Erythromycin can be effective in settling it down. You can see that the same list seems to be used in other skin conditions we do not regard as primary infections, including acne and rosacea. These antibiotics seem to exert an anti-inflammatory effect that

soothes all these conditions much in the manner of NSAIDs—that is why they are usually taken in lower doses than for infections and for a longer course.

**cme**

Answered by:

**Dr. Scott Murray**