Activity Levels Effect on Prenatal Glucose Tolerance Test

1. Does activity level during prenatal Glucose Tolerance Test (GTT) affect the results?

Question submitted by:
Dr. Kit Kitamura
Halifax, Nova Scotia

The formal 100g GTT is given to women who have screened positive on their antenatal glucose test or who are believed to be at risk for gestational diabetes. The test is to be done after three days of preparation: eating normally, including carbohydrates, and maintaining a normal exercise and activity level. Before the test, the patient is asked to fast at least ten hours, after midnight, and to refrain from excessive activity or exercise. Glucose serum values are then drawn at intervals between one to four hours after ingestion of a 100g glucose drink. During this testing phase, the patient is asked to be still and refrain from activity. Studies have shown that excessive exercise before or during this testing period can increase the level of blood glucose values due to impaired glucose tolerance. Thus, activity can interfere with the test results.

Answered by:
Dr. Cathy Popadiuk

Risk of Using PPIs Over a Long Period of Time

2. As achlorhydria can lead to gastric carcinoma, what is the risk of using PPIs over a long period?

Question submitted by:
Dr. Don Pinksen
Guelph, Ontario

Proton pump inhibitors (PPIs) can theoretically cause atrophic gastritis and achlorhydria. There is a concern that this could lead to gastric cancer. There has been one cohort study and one randomized controlled trial of patients taking omeprazole, which showed no association between PPI use and atrophic gastritis. Another cohort study of patients using omeprazole for one year showed an increase in atrophic gastritis. However, none of the studies showed an association between omeprazole use and intestinal metaplasia or its progression to gastric adenocarcinoma.

The available evidence indicates that PPI use is not clearly associated with atrophic gastritis. Long-term use of PPIs appears safe and no evidence clearly links PPIs to gastric cancer.

Answered by:
Dr. Jerry S. McGrath

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Antipsychotics for Aggressive Patients with Dementia

3. What do you think about combining typical and atypical antipsychotics for aggressive patients with dementia?

Question submitted by:
Dr. Carlo Milo
Atikokan, Ontario

Patients with dementia often require medication to manage behavioral and psychological symptoms, which can be very distressing to the individual, family and caregivers.

A recent review of the evidence in literature suggests that the atypical antipsychotics may have modest efficacy for the treatment of aggression in the short-term (*i.e.*, six to twelve weeks), but limited benefits in the long-term. There have also been safety concerns raised by governing bodies with respect to the second generation or atypical antipsychotics. Specifically, there have been "Black Box" warnings (1.6 times increased risk of stroke and/or death) issued for the use of atypical antipsychotics in patients with dementia (especially risperidone).

Trifiro *et al.* felt that based on their findings, typical antipsychotics as well should be included in the current FDA Black Box Warning. There have also been two additional studies that looked at the rate of stroke or transient ischaemic accidents in patients with dementia. Both studies found that the rates of stroke were equivalent between patients taking typical agents and those taking atypical agents.

It may be prudent to ask whether or not to even use typical and atypical antipsychotic agents in this vulnerable patient population. Additive receptor affinities specific to the medications, when used in combination, may negate the approach of smaller doses of two separate antipsychotic agents. This polypharmacy theory has its own challenges and should only be initiated once other pharmacological (*e.g.*, cholinesterase inhibitors, NMDA modulators, trazodone, *etc.*) and non-pharmacological approaches (*e.g.*, aromatherapy, music or pet therapy, *etc.*) have failed.

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

Effectiveness of Medication in Autism Spectrum Disorder

4. How effective is medication in autism spectrum disorder?

Question submitted by:
Dr. Len Grbac
Etobicoke, Ontario

Firstly, there are no drugs to treat the fundamental causes of autism spectrum disorder (ASD). This is largely due to the fact that the biological determinants of ASD have yet to be defined, claims to the contrary aside. However, drugs can be used to control some of the behavioural symptoms associated with ASD, and these drugs vary in terms of efficacy against these symptoms. Obsessive-compulsive symptoms in the context of ASD have been treated with serotonin-selective reuptake inhibitors (SSRIs) with variable results. Behavioural problems among children with ASD have been treated with antipsychotic drugs, with side effects being a major limitation for the use of older antipsychotics. Of the newer antipsychotics, risperidone appears to have the most promise, with good results in more than one study. Children with ASD who are high functioning are sometimes troubled by inattention, which is responsive to methylphenidate. Seizures, which can be a comorbidity of ASD, can be effectively managed using conventional anticonvulsants such as valproic acid or carbamazepine. Prescription drug use among children with ASD is common, and as many as 70% of children diagnosed with ASD are treated with at least one drug.

In children with ASD, the efficacy and safety of most drugs is not well established, and these children need to be carefully monitored to determine if a drug is producing the desired therapeutic effect, or if it may be producing undesired adverse effects.

Answered by:
Dr. Michael Rieder

Pap Testing in Women After Age 69

5. Why do we stop performing paps on women after age 69? If they are sexually active are they at risk of HPV infection?

Question submitted by:
Dr. D Petrovic
Burnaby, BC

Many cervical cancer screening guidelines suggest a stop date for screening, such as 69-years-old. This is in the context of a woman having undergone regular screening in her lifetime and having no history of dysplasia or a worse abnormality. If this is not the case or the Pap smear history is not known, then a woman should undergo screening until she has had three normal Pap smears consecutively on an annual basis. At this point screening interval may be increased or discontinuation considered in the senior female. Practically, a woman over 69 may encounter a new partner(s) after discontinuation of Pap smears in the context of a normal screening history. Theoretically, she would be at risk of exposure to HPV and its potential consequences. It is thus not unreasonable to offer Pap smear screening to senior women in this situation.

Answered by:
Dr. Cathy Popadiuk

Diagnosis of Mesenteric Adenitis

6.

Please comment on the diagnosis of mesenteric adenitis. It is often seen in kids being evaluated for possible appendicitis.

Question submitted by:
Dr. Laura McConnell
Mississauga, Ontario

Mesenteric adenitis is a self-limited inflammatory process in the right lower quadrant. It affects the mesenteric lymph nodes and clinically mimics acute appendicitis. Diagnosis is often made when a laparotomy is performed to assess for presumed appendicitis. Now it is often detected when diagnostic imaging is applied in the examination of patients with abdominal pain.

It is most frequently caused by viral pathogens, but other infectious agents have been implicated, such as *Yersinia enterocolitica*, *Helicobacter jejuni, Campylobacter jejuni,* and *Salmonella* or *Shigella* species. In toddlers and infants an ileocolitis may be present as well.

Most cases are self-limited, although disease lasting longer than two weeks is not uncommon. It is characterized by fever, abdominal pain, nausea and occasionally, diarrhea. Pain and tenderness often mimic appendicitis and are usually centered in the right lower quadrant, but they may be more diffuse than in appendicitis. The diagnosis is one of exclusion, and management is conservative. Ultrasonography of the right lower quadrant with graded compression has been the mainstay of diagnosis. Alternatively, CT imaging can be used.

Answered by:
Dr. Jerry S. McGrath

Prevention of Tonsilloliths

7.

Is there any way to prevent tonsilloliths?

Question submitted by:
Dr. Otto Mann
Dartmouth, Nova Scotia

Tonsilloliths consist mainly of debris (food, dead bacteria, immune cells, and crypt epithelial cells) that accumulate in the crypts (or pockets) of the pharyngeal tonsils. They are irritating if they become large due to their obstruction of the tonsillar crypts, and may produce a localized inflammation. Some authors believe that they contribute to halitosis. They can be carefully removed using a cotton swab dipped in listerine or hydrogen peroxide. Gargling with warm salt water has been suggested as a way to prevent the formation of tonsilloliths. Treating bacterial tonsillitis may prevent the scarring that occurs in the tonsillar tissue and subsequent crypt formation. However, antibiotics per se are usually ineffective. Cautery with topical silver nitrate has been recommended in adults. Tonsillectomy is always successful in curing this problem.

Answered by:
Dr. Ted Tewfik

Treatment of Patients with Hashimoto's Thyroiditis

8.

When should we treat patients with Hashimoto's thyroiditis?

Question submitted by:
Dr. Sakina Raj
Calgary, Alberta

Patients with Hashimoto's thyroiditis generally require treatment when they have a hypothyroid. In general, treatment is recommended if the TSH is greater than 10 mIU/L and/or if the patient is symptomatic.

In patients who have subclinical hypothyroidism (TSH between 5.0 to 10.0 mIU/L), it is somewhat controversial whether treatment is indicated or beneficial.

Answered by:
Dr. Hasnain Khandwala

C. difficile Relapse Treatment

9.

If a patient who has already been treated for *C. difficile* relapses with symptoms and has a positive test result again, when should we treat with vancomycin or a longer course of metronidazole?

Question submitted by:
Dr. Bhoama Bhayane

For relatively mild cases, there is no evidence to suggest that the relapse rate after treatment of *C. difficile* infection is significantly different when either metronidazole or vancomycin is used, or that switching regimens results in a lower relapse rate than repeating treatment with the same drug. Prolonging the course of either agent, typically with some form of gradual tapering of dosing, does appear to lower the relapse rate, based on limited data. Many experts use a six week course, with either gradually diminishing doses, or alternate day dosing at the end of treatment. There also seems to be some preference for using vancomycin in these cases, but there is no data to support this. There is now fairly good evidence that in the case of severe disease, vancomycin has a better primary response rate than metronidazole. Encouragingly, there are new agents in development, which appear to have lower relapse rates than either of these traditional treatments. In addition, there is some encouraging new data on the possibility of a vaccine.

Answered by:
Dr. Michael Libman

Lipid-lowering Agents

10.

At what age can we discontinue lipid-lowering medications?

Question submitted by:
Dr. Roback
Victoria, BC

The bias against prescribing statins for older individuals stems from concerns regarding life expectancy, comorbidity, safety of statins, and cost-benefit ratio. In fact the absolute risk for coronary heart disease increases dramatically with age. Thus the absolute number of persons benefiting from statin treatment should be greater among the elderly.

Elderly patients were under-represented in post-myocardial infarction (MI) statin trials. Despite that, post-hoc analyses showed patients above 65-years-of-age benefited from statin as much as those who were younger. On the other hand, there is only limited evidence for primary prevention among older patients without established cardiovascular diseases.

Statins have been shown to be significantly underutilized among otherwise eligible elderly patients. Elderly individuals without significant concomitant illness that would limit their life span should not be denied statin therapy based on their age alone.

Answered by:
Dr. Chi-Ming Chow

Chronic *Salmonella* “Non-typhoid” in Stool and Chronic Diarrhea

11.

What to do with a patient with chronic *Salmonella* "non-typhoid" in stool with chronic diarrhea?

Question submitted by:
Dr. Michael Manjos
Jordan, Ontario

As opposed to typhoid, non-typhoid *Salmonella* rarely results in chronic infection. The average carrier period is about two months after illness (or treatment). Antibiotic therapy does not reduce this carrier period. However, a small percentage of patients do become carriers, usually without symptoms. Regimens which have been used to eliminate carriage include ciprofloxacin for one month, and amoxicillin or co-trimoxazole for three months. Efficacy is close to 80%. Cholecystectomy may help in the presence of stone-related carriage. Chronic symptomatic infection likely indicates significant immune dysfunction, and is particularly prevalent in advanced HIV infection. The latter may require life-long antibiotic suppression, unless a patient recovers immune function in the course of his/her HIV treatment. Finally, there is always the possibility of chronic diarrhea due to another pathology, with incidental carriage of *Salmonella*.

Answered by:
Dr. Michael Libman

Multiuse Vitamins Containing Folic Acid and Risk of Malignancies

12.

Can multiuse vitamins which contain folic acid increase the risk of hematologic malignancies?

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

Folate is a B vitamin essential for DNA synthesis, methylation, and repair. Folic acid, the synthetic form, is used in isolation or in multivitamin supplements. The role of folate in cancer prevention has been described in population based studies. However, recent large randomized trials have not confirmed these findings and have further raised concerns that folic acid supplementation can potentially increase the risk of malignancies. The majority of higher risk subgroups are lung, colon, or prostate cancer, not necessarily hematologic malignancies. However, further clinical trials will be required to tease out if multiuse vitamins containing folic acid do not increase the risk of hematologic malignancies, and if so, at what duration, exposure levels, and with what concomitant risks.

It is important to understand that folic acid supplementation is important to reduce neural-tube birth defects and for replacement therapy in patients with folate deficiency. The risk of malignancies in these settings is not known.

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

Drug-eluting Stent for Patients on Clopidogrel

13. Should we consider keeping patients with drug-eluting stent (DES) on clopidogrel indefinitely?

Question submitted by:
Dr. Alan Payilanis
Montreal, Québec

An advisory board with members from the American Heart Association (AHA), the American College of Cardiology (ACC), the Society of Cardiac Angiography (SCAI) the American Cancer Society (ACS) and the American Diabetes Association (ADA) published a document in 2007 (Circulation 2007;115) stressing the importance of 12 months of dual antiplatelet therapy (ASA and clopidogrel) after placement of a drug-eluting stent (DES). Moreover, they emphasize the importance of educating the patient and healthcare providers about hazards of premature discontinuation of ASA and clopidogrel. The advisory board also recommends postponing elective surgery for one year, or considering the continuation of ASA during the perioperative period in high-risk patients with DES if surgery cannot be deferred.

Some physicians recommend continuing clopidogrel beyond one year, or even indefinitely, as long as the drug is well-tolerated and expense is not an issue. This approach is primarily considered in patients with particularly severe vascular disease (*e.g.*, prior myocardial infarction, cerebrovascular event or peripheral vascular disease) based on data from the Clopidogrel versus ASA in Patients at Risk of Ischaemic Events (CAPRIE) trial.

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Answered by:
Dr. Chi-Ming Chow

Reader's Response

Is Conjugated Quadrivalent Meningococcal Vaccine Worthwhile?

I was surprised by Dr. Michael Libman's response to Dr. Choi's question about the meningococcal vaccine in the October issue of CME, Volume 22 No.10 entitled: "Is Conjugated Quadrivalent Meningococcal Vaccine Worthwhile?" Here is the table from IMAPACT's statistical collection.

Submitted by:
Dr. Kathleen Ross
Winnipeg, Manitoba

Pneumococcal Invasive Infections

Table 7: Children with pneumococcus by year of admission and age, 2004 to 2008

Age	2004	2005	2006	2007	2008
0-5 mo	22	18	20	20	16
6-23 mo	138	68	49	55	54
2-4 yr	86	48	27	50	52
5-9 yr	34	37	33	32	28
>=10 yr	11	11	13	16	19
Total	291	182	142	173	169

Meningococcal Invasive Infections

Table 8a: Locally defined serogroup by year, 2004 to 2008

Serogroup	2004	2005	2006	2007	2008
A	1	0	0	0	0
B	39	41	52	62	26
C	22	15	15	12	7
W-135	2	3	1	8	3
Y	17	13	12	14	6
Untypeable	2	0	1	1	0
Unknown/not done	8	3	2	11	2
Total	91	75	83	108	44

W135 + Y combined account for more cases than C

Of the seven serogroup C infections in 2008, four occurred in adults older than 19-years-of-age and three occurred in children younger than 19-years-of-age.

Author's Reply

My previous statement that Type C meningococcal disease is heavily predominant is not correct. In recent years, although Type C remains the single most common vaccine-preventable serotype overall, some parts of Canada are seeing shifts similar to those observed in the USA. In particular, type Y and to a lesser extent type W-135 have been increasing in prevalence. It is possible that some provinces, based on their local epidemiology, will judge the cost-benefit ratio for the quadravalent vaccine to be acceptable from a public policy standpoint. The decline in type C disease may reflect widespread vaccination against type C, although this was not widely adopted in the US. Our major problem remains type B disease, and fortunately there has been good progress in the development of a type B vaccine.

Answered by:
Dr. Michael Libman