Nitrosamines

Description/Etiology
Nitrates and nitrites are naturally occurring byproducts of oxidized ammonia that are released through the decomposition of animal wastes and contents of septic systems, and the use of fertilizer. Nitrates are also found in broccoli, cauliflower, collard greens, and root vegetables, as well as in food preservatives. Nitrates are more prevalent than nitrites, though both are present in a variety of mediums and environments, including industry, agriculture, and medicine. Although not considered toxic, nitrates can contribute to nitrite toxicity because the body can convert nitrates into nitrites.

Nitrates and nitrites are capable of causing serious harm through poisoning. In toxic amounts, they relax smooth muscle, which causes vasodilation, and oxidize hemoglobin to methemoglobin, which results in hypoxia and cyanosis. This can cause orthostatic hypotension, dizziness, and/or headache, which can negatively affect appetite and dietary intake. Metabolic acidosis develops in nitrite poisoning. The body usually excretes excess nitrates and nitrites in the urine, but in extreme cases of poisoning, treatment with the application of 100% oxygen and methylene blue is necessary to reduce methemoglobin to hemoglobin. Methylene blue is not effective in patients with glucose-6-phosphate dehydrogenase deficiency, and blood transfusion may be necessary for effective treatment in this population.

There is speculation among clinicians that nitrates and nitrites have carcinogenic properties due to their contribution to the formation of nitrosamines. Nitrosamines, formed from nitrates and secondary amines, are known carcinogens for much of the animal kingdom. Although there is some evidence that they are associated with gastric, esophageal, and nasopharyngeal cancers and brain tumors, research regarding a causative role of nitrosamines in human cancers is not definitive.

Facts and Figures
While the role of nitrosamines in cancer risk is uncertain, the American Institute for Cancer Research (AICR) states that many types of cancer are associated with excess body fat. AICR estimates that 49% of endometrial cancers, 35% of esophageal cancers, 28% of pancreatic cancers, 24% of kidney cancers, 21% of gallbladder cancers, 17% of breast cancers, and 9% of colorectal cancers are linked to excess body fat.

Risk Factors
There is ample evidence that risk of certain cancers (e.g., stomach, esophageal) is increased with the consumption of processed meats and fried foods, which tend to have higher nitrate/nitrite/nitrosamine content. There are also some research results that suggest that higher maternal intake of nitrates/nitrites during pregnancy may be associated with greater risk, to the fetus, of future childhood cancers. Smokers are at a significantly higher risk for developing cancer than non-smokers due to the high nitrosamine content of tobacco.

Signs and Symptoms/Clinical Presentation
Nitrate or nitrite poisoning manifests with orthostatic hypotension, syncope, tachycardia, flushed skin, cyanosis, headache, dizziness, and/or tachypnea; if untreated, it can progress to lethargy, stupor, coma, seizures, metabolic acidosis, and cardiovascular collapse.
Signs and symptoms of cancer vary according to the type of cancer, although there are standard warning signs of increased risk of diet-related cancer (e.g., hypertension, diabetes mellitus, heart disease, liver or kidney disease, intestinal disorders).

**Nutritional Assessment**

› **Patient Medical History**
  - Ask about the onset and details of signs and symptoms (e.g., orthostatic hypotension, dizziness, headache), which can negatively affect dietary intake
  - Ask about glucose-6-phosphate dehydrogenase deficiency and other medical conditions (e.g., renal or cardiac failure, chronic obstructive pulmonary disease[COPD])
  - Ask about nitrite inhalant use
  - Ask about personal habits (e.g., physical activity, alcohol consumption, smoking), including about nitrite inhalant abuse, as these can result in higher levels of nitrites/nitrates/nitrosamines

› **Physical Findings of Particular Interest**
  - Nitrite poisoning can cause the blood to be a chocolate brown color due to the presence of methemoglobin

› **Patient Dietary History**
  - Conduct a diet analysis by asking the patient to complete a diet history (assess for dietary intake of nitrate, nitrite, and nitrosamine)
    – Useful tools for evaluating the patient’s dietary strengths and weaknesses include a food frequency questionnaire and a 3-day diet recall (i.e., patient recall of all foods and beverages consumed in a 3-day period) that includes 1 weekend day
  - Assess for anxiety and depression, which can interfere with dietary intake

› **Anthropometric Data**
  - Calculate the patient’s body mass index (BMI) by dividing body weight (kilograms) by the square of height (meters) or 703 multiplied by weight (pounds) and divided by the square of height (inches)
    – Underweight: < 18.5 kg/m^2; Normal: 18.5–24.9 kg/m^2; overweight: 25–29.9 kg/m^2; obese: > 30 kg/m^2
  - In patients older than 65 years, evidence suggests that a slightly higher BMI (25–27 kg/m^2) may help prevent bone deterioration and is associated with a lower risk of mortality
  - In some cases, body composition testing (e.g., dual-energy x-ray absorptiometry scan, skin calipers) may be necessary

› **Laboratory Tests and Diagnostic Tests of Particular Interest to the Nutritionist**
  - Co-oximetry, a spectrophotometric method for differentiating the various types of hemoglobin, is the best tool for definitive diagnosis of nitrite poisoning

**Treatment Goals**

› **Promote Optimum Physiologic Status, Reduce Risk of Complications, and Educate**
  - Review the results of laboratory tests and diagnostic studies used to assess for or monitor complications related to nutritional status; report findings to the treating clinician as they are obtained
  - Assess patient/family anxiety level, coping ability, and for knowledge deficits regarding the diagnosis; provide emotional support
  - Review diet history information to assess dietary intake and patterns, and provide detailed patient education regarding diet and nitrite poisoning
  - As appropriate, request referral to a social worker for identification of local programs for drug abuse, support groups, and/or additional information

**Food for Thought**

› Consumption of cured meats has been associated with a heightened risk of COPD, although it is not known if the meat consumption causes COPD. However, nitrite in exhaled breath condensate can be used as a marker of nitrosative stress (i.e., high levels of nitrous oxide) in adult patients with lung diseases (e.g., asthma, COPD)
  - Smoking and using smokeless tobacco during pregnancy in Alaska Native women are linked to a moderate to strong fetal exposure to tobacco-specific carcinogens (4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol or NNAL). Researchers hope that this evidence will encourage pregnant Alaska Native women to stop using tobacco (Flanagan et al., 2016)

**Red Flags**

› Infants receiving formula mixed with tap water are at increased risk for nitrate/nitrite poisoning
What Do I Need to Tell the Patient/Patient’s Family?

› Eat a well-rounded diet that includes a variety of fruits, vegetables, whole grains, and lean proteins. For more information, see the USDA’s food guidance system, Choose MyPlate at http://www.choosemyplate.gov/
› Strict treatment regimen adherence and continued medical surveillance is vital to prevent complications

Discharge Planning

› Eat a calorie-appropriate diet that includes fish and other lean proteins, unsaturated fats (including omega-3), complex carbohydrates (e.g., unrefined wholegrains), legumes, nuts and seeds, and a variety of fruits and vegetables
› Participate in regular physical activity of at least 150 minutes each week, including strength training at least 2 days each week, if medically appropriate

References