Cancer of the pancreas -- Nutritional therapy

Nutritional therapy and Supplements

Long-Term Survival with Alpha-Lipoic Acid (Intravenous), Multiple Antioxidants, and Low-Dose Naltrexone

A recent case report describes the long-term survival (>3 years) of a 46-year-old man who was diagnosed with a very aggressive cancer of the pancreas (adenocarcinoma) which had spread to the liver. The patient had a 3.9 x 3.9 cm tumor in the head of the pancreas and 4 tumors in the liver, one of which was 5 to 6 cm in diameter. He was told there was not much that could be done for him, yet he was treated with one round of a typical chemotherapy regimen (Gemzar® (gemcitabine) and Paraplatin® (carboplatin)), which caused reduced blood cell counts but no tumor regression. He received a second opinion that any further treatment would be in vain, so he opted for an integrative medical approach (via the Integrative Medical Center of New Mexico).

For his non-cancer medical conditions he was given several antacids (Prevacid® 30 mg, Rolaids®), antibiotics (Primsolv™/Gantanol®), anti-ulcer agents (Mylanta®, Pepto-Bismol®), and the anti-anxiety drug, Xanax®, and then he started an integrative therapy program, the ALA-LDN (Intravenous Alpha-Lipoic Acid- Low-Dose Naltrexone) protocol.

The ALA-LDN protocol comprised alpha-lipoic acid (ALA) (300 to 600 mg intravenously twice weekly), low-dose naltrexone (Vivitrol™) (3 to 4.5 mg at bedtime), and orally, ALA (300 mg twice daily), selenium (200 micrograms twice daily), Silymarin (300 mg four times daily), and vitamin B complex (3 high-dose capsules daily). In addition, he maintained a strict dietary regimen, performed a stress-reduction and exercise program, and led a healthy lifestyle. Remarkably, after just one treatment of intravenous ALA his symptoms began to disappear, his quality of life improved, and he had no unwanted side effects.
His pancreatic cancer has remained stable for more than 3-years and he is free from symptoms. Several other patients are being treated with this protocol and, to date, with success. Thus, the ALA-LDN protocol could possibly extend the lives of those pancreatic cancer patients who have been led to believe that their cancer is terminal.

How Does It Work?

Alpha-lipoic acid is a potent antioxidant, improves immune cells’ functions, increases homocysteine levels in cancer cells which is toxic to them, and prevents the activation of nuclear factor kappaB a key regulator of tumor development and progression. Selenium is useful in elevating antioxidant levels and Silymarin is a selective COX-2 inhibitor.

Low-dose naltrexone blocks opiate receptors causing the body to make large amounts of opiates in response, which in turn improve the immune response; specifically, natural killer cell cytotoxicity, B-cell and T-cell proliferation, and IFN-gamma production are maintained during times of immune suppression.

Prevacid® is an antacid that also improves cell-mediated immunity, prevents immune suppression, and may also exert anti-inflammatory activity, all of which are important for cancer patients with impaired immune systems.

Pancreatic Enzyme Replacement Therapy

Dr. John Beard, who published The Enzyme Theory of Cancer in 1911, was the first to propose using pancreatic digestive enzymes to treat cancer. Later, Dr. William Donald Kelley treated his cancer patients with enzymes for more than 20 years, and many lived far beyond expectations. By comparison, in a trial of 126 pancreatic cancer patients treated with the drug Gemzar®, not one patient lived longer than 19 months. Treating patients with pancreatic extract containing enzymes resulted in significantly improved absorption in those with moderate-to-severe fat or protein malabsorption.
In a remarkable study by Dr. Nicholas Gonzalez, 11 patients with pancreatic cancer were treated with large doses of pancreatic enzymes, nutritional supplements, ‘detoxification’ procedures, and an organic diet. Of the 11 patients, nine survived for one year, five survived two years, and four survived three years. This pilot study suggests that aggressive nutritional therapy with large doses of pancreatic enzymes significantly increased survival over what would normally be expected for patients with inoperable pancreatic cancer. An experimental animal study found that treating tumors in mice with pancreatic enzyme extract (PPE) significantly prolonged their survival and slowed tumor growth.

As a result of the pilot study, the National Cancer Institute and the National Center for Complementary and Alternative Medicine approved funding for a large-scale phase III clinical trial comparing Dr. Gonzalez’s nutritional regimen against Gemzar® in treating inoperable pancreatic cancer. This study has full FDA approval and is being conducted under the Department of Surgical Oncology at New York Presbyterian Hospital, Columbia Campus (www.clinicaltrials.gov).

Several factors contribute to the effectiveness of pancreatic enzyme replacement therapy. These include:

- Patient compliance and adherence to scheduled dose and timing of intake.
- Individual weight perception versus actual weight measurement.
- Type of pancreatic enzyme preparations, that is, pancrelipase powder versus enteric-coated products. Delayed-release preparations (capsules containing enteric-coated microspheres, such as Creon®) are reportedly less susceptible to acid inactivation in the stomach and duodenum, as they are designed to disintegrate at a relatively high gastrointestinal pH (greater than 5.5 to 6).
- Antacids or a histamine H2-receptor antagonist (cimetidine, Tagamet®) have been used to decrease the inactivation of enzyme activity.
Nutritional intervention aims to:

- Reduce the occurrence of pancreatic cancer.
- Decrease treatment-related disease and deaths.
- Enhance response to radiation and chemotherapy.
- Improve long-term survival via direct therapeutic effects.

Consuming a diet rich in fruits and vegetables, plus controlling calories by dietary measures or exercise, are measures that will help to prevent the spread of pancreatic cancer. A constituent of cruciferous vegetables such as watercress called phenethyl isothiocyanate (PEITC) stopped pancreatic cancer from developing in a hamster model that was given a cancer-causing agent (a carcinogen known as BOP).

**Monoterpenes**

Monoterpenes are found in the essential oils of citrus fruits and other plants. The monoterpenes limonene and perillyl alcohol demonstrate intense antitumor activity against pancreatic cancer cells. They counter cancer by:

- Jump-starting enzymes that are able to break down cancer-causing chemicals.
- Preventing cancer cell growth by reducing RAS activity and causing cancer cell death.
- Restraining liver enzyme actions (hepatic HMG-CoA reductase activity), which controls cholesterol production and thus cancer cell growth.

**Limonene**

Found in citrus fruits, limonene reduces the growth of pancreatic cancer cells by 50 percent. The tentative dose recommendation for limonene is 7.3 to 14.4 grams per day. According to studies, limonene is well tolerated in cancer patients at doses that may have clinical activity. One partial response in a breast cancer patient at a dose of 8 grams taken twice daily was maintained for 11 months, and three additional patients with
colorectal cancer showed disease stabilization for longer than six months on d-limonene at 0.5 or 1 gram taken twice daily.

*Perillyl Alcohol.*

Perillyl alcohol is found in small concentrations in the essential oils of lavender, peppermint, spearmint, sage, cherries, cranberries, perilla, lemongrass, celery, and caraway seeds. Perillyl alcohol exhibits powerful effects in minimizing cancer cell growth and preventing the mutated RAS proteins from continuously stimulating cancer cell growth.

- Twelve clinical trials have investigated the use of perillyl alcohol in various types of cancer treatments. A 2050-mg dose administered four times daily was found to be easily tolerated. In one clinical trial, perillyl alcohol was administered four times a day to 16 patients with advanced cancers not responding to treatment. Evidence of antitumor activity was seen in a patient with metastatic colorectal cancer who had an ongoing near-complete response of greater than two years’ duration. Several patients had stable disease for as long as or greater than six months. The predominant toxicity of perillyl alcohol seen during most trials was gastrointestinal (nausea, vomiting, and belching), limiting the dose. The minimum required antitumor dose is 1.3 grams per day.

*Gamma Linolenic Acid (GLA)*

GLA, a fatty acid found in borage oil, slows the growth and spread of pancreatic cancer by hindering tumor blood-vessel development. GLA treatment changes tissue blood flow dramatically in pancreatic tumors, even at low doses.

*Fish Oil*

Patients with advanced pancreatic cancer usually experience weight loss (catabolic wasting or cachexia) and often fail to gain weight with
conventional nutritional support. EPA, an essential fatty acid found in fish oil, restrains pancreatic cancer cell growth in laboratory experiments at low doses and decreases the number of cancer cells at higher doses. The maximum tolerated daily dose of fish oil was found to be 0.3 grams per kilogram (kg) of body weight. This means that a 70-kg (154-lb.) patient can generally tolerate up to 21 grams of fish oil containing 13.1 grams of EPA and DHA (Burns CP et al 1999). However, in a phase I study of five pancreatic cancer cachexia patients, a mean dose of approximately 18 grams per day (doses ranged from 9 to 27 grams per day) of a new high-purity preparation of EPA as a 20 percent oil and water diester emulsion was tolerated.

Several studies have shown that supplementation with fish oils containing EPA and DHA is helpful and may even reverse weight loss caused by cancer. Moreover, consumption of a protein- and energy-dense oral nutritional supplement containing omega-3 fatty acids (such as EPA) improves body weight, lean body mass, and quality of life in patients undergoing chemotherapy.

Fish oil supplements providing at least 2400 mg of EPA and 1800 mg of DHA daily have been recommended. To reduce cachexia, an estimated 2 to 12 grams per day of EPA is needed.

Clinical Studies: Fish Oil and Pancreatic Cancer

Many clinical studies have shown that fish oil supplementation stabilizes the rate of weight loss, as well as adipose tissue and muscle mass, in pancreatic cancer patients, who often suffer from wasting.

- Protein supplements enriched with EPA increased total energy expenditure and physical activity levels in advanced pancreatic cancer patients, thereby increasing their quality of life.
- Twenty pancreatic cancer patients were asked to consume two cans of a fish oil-enriched nutritional supplement daily in addition to their normal food intake. Each can contained 16.1 grams of protein and 1.09 grams of EPA. At the study’s onset, all patients were losing weight at a median rate of 2.9 kg a month.
After administration of the fish oil-enriched supplement, patients had a significant weight gain at both three and seven weeks.

- In another study, after three weeks of consuming an EPA-enriched supplement, the body weight of cancer patients had increased, and their energy expenditure in response to feeding had risen significantly to levels no different from baseline healthy control values.
- In a study of 18 pancreatic cancer patients who supplemented with fish oil capsules (1 gram each containing EPA 18 percent and DHA 12 percent), patients had a median weight loss of 2.9 kg a month before supplementation; three months after beginning fish oil supplementation, patients had a median weight gain of 0.3 kg a month.

**Food-Derived Polyphenols**

*Genistein*

Genistein prevents pancreatic cancer cell growth primarily by regulating sugar metabolism. In addition, genistein inactivates NF-kappa B, thus sensitizing cancer cells to chemotherapeutic agents such as Gemzar®, cisplatin and docetaxel, and VP-16 and doxorubicin. In laboratory experiments, genistein has been shown to improve survival, reduce tumor blood-vessel development, almost completely inhibit cancer metastasis, and increase cancer cell suicide.

If the pathology report shows that the pancreatic cancer cells have a mutated p53 oncogene, or if there is no p53 detected, then high-dose genistein therapy may be appropriate. If the pathology report shows a functional p53, then genistein is less effective in stopping cancer growth. The suggested dose of genistein is approximately 500 mg daily.

*Green Tea*

Tea is particularly rich in polyphenols such as epigallocatechin gallate (EGCG) that act as antioxidants. Black and green tea extracts reduce pancreatic tumor cell growth by approximately 90 percent while...
preventing angiogenesis. They also decrease the expression of the K-ras gene and the invasiveness of pancreatic cancer cells. Animal experiments of pancreatic cancer show that tea polyphenols restrain carcinogen-induced increases in oxidative DNA damage.

Green tea extract curbs the process of pancreatic cancer development and the promotion of transplanted human pancreatic cancer in animals, and also causes pancreatic cancer cell death.

In humans, an inverse relationship was observed between the amount of green tea consumed and the risk of developing pancreatic cancer; the highest intake was associated with the lowest risk of cancer (Ji BT et al 1997). In clinical studies, green tea supplementation has been shown to be safe and protective.

Antioxidants

Free radicals can cause repeated damage to normal cells and reduce the function of injured tissues. When sufficient antioxidants are available, free radicals are removed before excess damage occurs. Antioxidant levels are reduced in pancreatic cancer compared to other pancreatic diseases and healthy pancreatic tissue, resulting in increases in reactive oxygen that are capable of stimulating cancer cell division.

Increased levels of some antioxidants may be useful in slowing the growth of pancreatic cancer. Vitamins A, C, and E, as well as selenium, increase antioxidants in the body needed to reduce free-radical damage.

Vitamins A, C, and E

In animals in which pancreatic cancer was caused by chemicals, cancer incidence was decreased by 64.3 percent by vitamin A and by 71.4 percent with vitamin C. Both vitamins increased SOD (superoxide dismutase) activity and were toxic to tumor cells but not to normal healthy cells.
• An overview of 14 randomized trials (with a total of 170,525 patients) showed significant effects of supplementation with beta-carotene, vitamins A, C, E, and selenium (alone or in combination) versus placebo on pancreatic cancer incidence.

• A study of 23 pancreatic cancer patients tested retinol palmitate (vitamin A) and beta-interferon with chemotherapy. Eight patients responded and eight patients had stable disease. For all patients, median time to disease progression and survival time were 6.1 months and 11 months, respectively. Toxicity was high, but patients who had responses and disease stabilization had prolonged symptom relief.

• Retinoids curb the growth and adhesion of a variety of pancreatic cancer types, even those that previously have been documented to be resistant to retinoids. Vitamin E succinate restrained pancreatic cancer cell growth in laboratory experiments.

• Ascorbyl stearate, a fat-soluble form of ascorbic acid (vitamin C), markedly restrained the growth of—and even killed—pancreatic cancer cells.

Selenium

Selenium and beta-carotene were found to restrain the growth of pancreatic tumors caused by carcinogen exposure in mice. Selenium levels were found to be reduced in pancreatic cancer patients who underwent surgery to remove the upper portion of their intestine. In preclinical studies, a diet high in selenium reduced the number of carcinogen-induced pancreatic cancers significantly.

Curcumin

Curcumin has many anticancer effects. It is a selective inhibitor of the COX-2 enzyme and may be beneficial in preventing and treating pancreatic cancer. It decreases NF-kappa B activity, which is involved in controlling the growth of pancreatic cancer cells. It also inhibits
interleukin-8 (IL-8) production, which affects invasiveness, cell growth, and tumor blood-vessel development.

- Aged Garlic Extract—1200 milligram (mg) daily
- Alpha-tocopherol—400 international units (IU) daily
- Ascorbic acid—500 to 3000 mg daily
- Beta-carotene—20 mg daily
- Curcumin—2400 mg daily, two hours apart from medications
- d-Limonene—7.3 to 14.4 grams (g) daily
- Fiber—4 to 12 g daily before meals
- Fish oil concentrate—700 to 4200 mg of EPA, 500 to 2000 mg of DHA daily
- Gamma-linolenic acid (GLA)—700 to 900 mg daily
- Grape seed extract—100 mg daily
- Green tea extract (EGCG)—800 mg daily
- Mix multivitamin/multi-mineral formula without copper—follow label directions
- Lycopene—15 to 30 mg daily
- Perillyl alcohol—2050 mg, four times daily
- PSK (Coriolus versicolor)—3 grams daily
- Selenium—600 micrograms (mcg) daily
- Silymarin—100 to 420 mg daily
- Soya extract (genistein)—656 mg daily
- Vitamin A—10,000 IU daily
- Zinc—45 to 50 mg daily

Pancreatic Cancer Safety Caveats

An aggressive program of dietary supplementation should not be launched without the supervision of a qualified physician. Several of the nutrients suggested in this protocol may have adverse effects if overdosed. These include:

Beta-Carotene
• Do not take beta-carotene if you smoke. Daily intake of 20 milligrams or more has been associated with a higher incidence of lung cancer in smokers.
• Taking 30 milligrams or more daily for prolonged periods can cause carotenoderma, a yellowish skin discoloration (carotenoderma can be distinguished from jaundice because the whites of the eyes are not discolored in carotenoderma).

**Curcumin**

• Do not take curcumin if you have a bile duct obstruction or a history of gallstones. Taking curcumin can stimulate bile production.
• Consult your doctor before taking curcumin if you have gastroesophageal reflux disease (GERD) or a history of peptic ulcer disease.
• Consult your doctor before taking curcumin if you take warfarin or antiplatelet drugs. Curcumin can have antithrombotic activity.
• Always take curcumin with food. Curcumin may cause gastric irritation, ulceration, gastritis, and peptic ulcer disease if taken on an empty stomach.
• Curcumin can cause gastrointestinal symptoms such as nausea and diarrhea.

**EPA/DHA**

• Consult your doctor before taking EPA/DHA if you take warfarin (Coumadin). Taking EPA/DHA with warfarin may increase the risk of bleeding.
• Discontinue using EPA/DHA two weeks before any surgical procedure.

**Fiber**

• Take fiber supplements with a full 300 ml of water.
• Drink 3-4 ltrs of water daily while taking fiber.
Garlic

- Garlic has blood-thinning, anti-clotting properties.
- Discontinue using garlic before any surgical procedure.
- Garlic can cause headache, muscle pain, fatigue, vertigo, watery eyes, asthma, and gastrointestinal symptoms such as nausea and diarrhea.
- Ingesting large amounts of garlic can cause bad breath and body odor.

Genistein

- Consult your doctor before taking genistein/genistin if you have prostate cancer.
- Do not take genistein/genistin if you have estrogen receptor–positive tumors.
- Genistein/genistin can cause hypothyroidism in some people.

GLA

- Consult your doctor before taking GLA if you take warfarin (Coumadin). Taking GLA with warfarin may increase the risk of bleeding.
- Discontinue using GLA two weeks before any surgical procedure.
- GLA can cause gastrointestinal symptoms such as nausea and diarrhea.

Green Tea

- Consult your doctor before taking green tea extract if you take aspirin or warfarin (Coumadin). Taking green tea extract and aspirin or warfarin can increase the risk of bleeding.
- Discontinue using green tea extract two weeks before any surgical procedure. Green tea extract may decrease platelet aggregation.
• Green tea extract contains caffeine, which may produce a variety of symptoms including restlessness, nausea, headache, muscle tension, sleep disturbances, and rapid heartbeat.

**Selenium**

• High doses of selenium (1000 micrograms or more daily) for prolonged periods may cause adverse reactions.
• High doses of selenium taken for prolonged periods may cause chronic selenium poisoning. Symptoms include loss of hair and nails or brittle hair and nails.
• Selenium can cause rash, breath that smells like garlic, fatigue, irritability, and nausea and vomiting.

**Vitamin A**

• Do not take vitamin A if you have hypervitaminosis A.
• Do not take vitamin A if you take retinoids or retinoid analogues (such as acitretin, all-trans-retinoic acid, bexarotene, etretinate, and isotretinoin). Vitamin A can add to the toxicity of these drugs.
• Do not take large amounts of vitamin A. Taking large amounts of vitamin A may cause acute or chronic toxicity. Early signs and symptoms of chronic toxicity include dry, rough skin; cracked lips; sparse, coarse hair; and loss of hair from the eyebrows. Later signs and symptoms of toxicity include irritability, headache, pseudotumor cerebri (benign intracranial hypertension), elevated serum liver enzymes, reversible non-cirrhotic portal high blood pressure, fibrosis and cirrhosis of the liver, and death from liver failure.

**Zinc**

• High doses of zinc (above 30 milligrams daily) can cause adverse reactions.
• Zinc can cause a metallic taste, headache, drowsiness, and gastrointestinal symptoms such as nausea and diarrhea.
• High doses of zinc can lead to copper deficiency and hypochromic microcytic anemia secondary to zinc-induced copper deficiency.
• High doses of zinc may suppress the immune system. High doses of zinc may be immunosuppressive.

**Blood and Cytology Tests**

Currently, there is no simple blood test that exists solely to detect or diagnose early pancreatic cancer. However, there are certain blood tests that can support a diagnosis of pancreatic cancer, or help your doctor determine treatment if evidence of cancer is found. None of these tests can be used as conclusive diagnostic tools on their own.

**Hepatic Function Test**

The hepatic function test will be a standard component of your blood work up and will test your bilirubin and enzyme levels. If there is a tumor blocking your bile duct, the bilirubin levels in your blood may increase and cause you to become jaundiced. The normal range of bilirubin levels is between 0.3mg/dL (milligrams per deciliter) and 1.3 mg/dL. Liver enzymes and pancreatic enzymes, such as amylase, may also be elevated as a result of a blocked bile duct.

**CA 19-9 Tumor Marker**

A tumor marker is a substance that may leak into the bloodstream and that can be produced by the tumor cell or by the body in response to the tumor cell. The levels of tumor markers in your bloodstream can help your doctor evaluate you for certain types of cancer.

CA 19-9 is a tumor marker commonly associated with pancreatic cancer. The normal range of CA 19-9 in the blood of a healthy individual is 0-37 U/mL (units/milliliter). People suffering from pancreatic cancer often have elevated levels of CA 19-9. However, it is important to note that not every patient with pancreatic cancer will have elevated levels of CA 19-9. Also, some non-cancerous conditions,
like pancreatitis and jaundice, can cause high levels of CA 19-9. Therefore, CA 19-9 cannot be used as a diagnostic or screening measure on its own.

If you are diagnosed with pancreatic cancer, your physician may use changes in your CA 19-9 levels to determine if your tumor is remaining stable, progressing, or responding to treatment. Your doctor may take a baseline CA 19-9 level before surgery or before beginning a cycle of chemotherapy. If the CA 19-9 levels decrease after treatment, that typically indicates a positive response. If after several cycles of chemotherapy your CA 19-9 levels remain the same that indicates your cancer is stable. If, however, your CA 19-9 levels rise, that can indicate either a recurrence of your cancer or that you are no longer responding to your current treatment plan.

*Carcinoembryonic Antigen (CEA)*

CEA is a protein that may also be used as a tumor marker. CEA is typically found in the blood of a developing fetus, but disappears almost entirely from the blood stream after birth. The normal range of CEA in an adult non-smoker is less than 2.5 ng/mL (nanograms per milliliter), and less than 5.0 ng/mL for an adult smoker. However, certain cancers like colorectal cancer and those involving the gastrointestinal tract are known to increase CEA levels in adults. CEA levels greater than 20 ng/mL before therapy are associated with metastatic cancer.

Similar to CA 19-9, CEA cannot be used as a diagnostic or screening test for pancreatic cancer because both cancerous and non-cancerous conditions can increase CEA levels. Smoking, certain infections, pancreatitis, and cirrhosis of the liver can all cause elevated CEA levels. Additionally, chemotherapy and radiation therapy can cause a temporary rise in CEA levels due to increased CEA release by tumor cells that are being destroyed.

Also similar to CA 19-9, the CEA test is best used to determine disease progression and treatment effectiveness. Your doctor may track the
changes in your CEA levels throughout your treatment if you are diagnosed with pancreatic cancer.

Additionally, if a cyst is found in the pancreas, a physician may aspirate, or pull fluid out, of the cyst to relieve symptoms and perform cytology tests. CEA levels found in the fluid can help your physician reach a diagnosis. Levels above 200 are worrisome.

Amylase and lipase tests are performed to aid in the differential diagnosis of acute abdominal pain. Amylase and lipase are digestive enzymes made by the pancreas. An enzyme is a protein that accelerates a biochemical reaction. Both enzymes are members of the hydrolase class, which means that they split a substrate by the addition of water. Amylase catalyzes the hydrolysis of starch forming maltose. The maltose can be converted to glucose by other enzymes. Lipase splits triglycerides, forming glycerol and fatty acids as the final product.

AFT (alpha fetoprotein) analysis should also be done.

**Purpose**

Epigastric pain and abdominal tenderness associated with acute appendicitis is difficult to distinguish from acute pancreatitis. Serial measurements of amylase and lipase are used to exclude a diagnosis of acute pancreatitis when results are within normal limits. One or both enzymes may be increased in acute pancreatitis, but neither enzyme is specific.

In addition to acute pancreatitis, amylase is increased in mumps, some malignancies, ectopic pregnancy, alcoholic liver disease, peptic ulcers, intestinal obstruction, and renal failure.

Lipase is increased in renal failure, intestinal obstruction and liver disease. Use of both enzymes increases diagnostic sensitivity and specificity to around 90%. Acute pancreatitis is highly likely when the plasma amylase is increased to more than twofold normal and lipase is increased more than fivefold normal. When plasma amylase is
increased, but the lipase is normal, a non-pancreatic condition is almost always the cause. When amylase is increased more than twofold and lipase is increased but less than fivefold, renal failure, pancreatitis, intestinal obstruction, peptic ulcer disease, and acute pancreatitis are possible causes.

In acute pancreatitis, plasma amylase becomes elevated two to 12 hours after an episode of acute abdominal pain. Levels peak in 12-72 hours, usually reaching two to six times the upper limit of normal, then return to normal by four days. Amylase is a small protein and is excreted in urine in significant quantities. Urinary amylase rises in parallel with plasma amylase, but reaches higher levels and remains elevated for seven to 14 days. Renal excretion of amylase is increased in pancreatitis, and the ratio of amylase to creatinine clearance is a more specific test for acute pancreatitis than is plasma amylase. Lipase in plasma becomes abnormal four to eight hours following an episode of acute pancreatitis, reaches a peak level two to 50 times normal in approximately one day, and remains elevated for seven to 10 days. Recently, serum and urine levels of trypsinogen-2 have been shown to be very sensitive and specific indicators of pancreatitis, but assays are not yet widely available.

**Precautions**

Blood for measurement of amylase and lipase is collected by venipuncture. The phlebotomist should follow standard precautions for the prevention of transmission of blood borne pathogens.

Amylase and lipase should not be used as screening tests for future pancreatic disease. Neither enzyme is likely to be elevated in chronic pancreatitis because enzyme production is decreased by chronic disease.

Up to 1% of persons have increased plasma amylase owing to formation of a complex between amylase and immunoglobulins. This condition is termed macroamylasemia and it occurs more frequently in the older population. Plasma amylase is elevated above normal, but
urinary amylase is low in this condition. The presence of natural amylase inhibitors in the diet may decrease plasma amylase activity. Drugs that may increase amylase include morphine, phenformin, ethanol, and contraceptives. Lipase may be increased by ethanol, codeine, and narcotics. Results are dependent upon the method used and normal values may vary significantly between laboratories.

Description

Amylase and lipase tests are usually performed on a blood sample, but amylase testing can also be performed on urine. Enzymes are usually measured by determining the rate of product formation under controlled pH and temperature. Measurements are reported as units of activity rather than in mass units. Reference methods for amylase and lipase are labor intensive and difficult to automate.

There are several methods for measuring amylase and lipase each with its own advantages and disadvantages.

A common method of measuring amylase is based upon the hydrolysis of a synthetic glucose polymer that is labeled at one end with p-nitrophenol. The amylase splits the substrate into various subunits of glucose. Subunits consisting of three glucose molecules are hydrolyzed by an enzyme in the reagent, alpha-glucosidase, forming glucose and p-nitrophenol. The activity of amylase is proportional to the rate of p-nitrophenol formation. This is determined by measuring the amount of light that the reaction mixture absorbs at 405 nm over a fixed time interval.

Lipase is often measured using a cascade of coupling enzyme reactions that yield a colored product. Lipase is incubated with a synthetic diglyceride substrate and splits it forming a monoglyceride and a fatty acid. The monoglyceride is split by an enzyme in the reagent, monoglyceride esterase, to yield glycerol. The glycerol is converted to glycerol-3-phosphate by the enzyme glycerol kinase which attaches a phosphate from adenosine-tri-phosphate (ATP). The glycerol-3-
phosphate is oxidized by another enzyme, glycerol phosphate oxidase (GPO), forming dihydroxyacetone phosphate and hydrogen peroxide. In the final step, peroxidase catalyzes the oxidation of a dye by the hydrogen peroxide forming a pink product. The rate of absorbance (color) increase at 500 nm is measured, and is proportional to lipase activity.

**Preparation**

No special preparation is necessary for a person undergoing an amylase or lipase test. Urinary amylase is frequently measured using a timed urine sample. The patient should be given a urine container with instructions for collecting the urine at home. The urine should be refrigerated until it is brought to the laboratory.

Amylase and lipase tests are not associated with complications.

**Results**

The normal range will vary depending upon the method used. Results shown below are representative of the methods described above performed at 37 degrees C.

- Plasma amylase: 70-200 U/L.
- Plasma lipase: 7-58 U/L.
- Urine amylase: Less than 1200 U/L.
- Amylase creatinine clearance ratio: 1-4%.

**Nutritional support**

Recently, there has been a shift in the management paradigm from TPN (total parenteral nutrition) to early, post-pyloric enteral feeding (in which a feeding tube is endoscopically or radiographically introduced to the third portion of the duodenum). The advantage of enteral feeding is that it is more physiological, prevents gut mucosal atrophy, and is free from the side effects of TPN (such as fungemia). The additional advantages of post-pyloric feeding are the inverse
relationship of pancreatic exocrine secretions and distance of nutrient delivery from the pylorus, as well as reduced risk of aspiration. Disadvantages of a naso-enteric feeding tube include increased risk of sinusitis (especially if the tube remains in place greater than two weeks) and a still-present risk of accidentally intubating the bronchus even in intubated patients (contrary to popular belief, the endotracheal tube cuff alone is not always sufficient to prevent NG tube entry into the trachea).