LIVS In Plain View

LONG ISLAND VETERINARY SPECIALISTS

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Inside This Issue

Canine Insulinomas

Catherine Loughin, DVM, Dip. ACVS, Dip. ACCT, Staff Surgeon

Insulinomas are pancreatic nodules that secrete excessive amounts of insulin leading xc xc to hypoglycemia. Other nodules that are frequently associated with paraneoplastic hypoglycemia include hepatomas, hepatocellular carcinomas, adenocarcinomas, leiomyomas, and leiomyosarcomas. There are three possible mechanisms of action that lead to hypoglycemia: secretion of insulin or insulin-like peptides, increased glucose utilization, or failure of hepatic glucose production. Commonly used drugs that may cause hypoglycemia include sulfonylureas (used to decrease blood glucose levels in diabetics), beta-blockers, and insulin overdose. A common toxin causing hypoglycemia in dogs is xylitol, an artificial sweetener found in some brands of sugar-free gum that stimulate an increase in insulin secretion. It can also cause delayed hepatic failure and secondary hypoglycemia.

Insulinomas arise from pancreatic beta cells. In dogs, approximately 60% of insulinomas are carcinomas; the remainder are adenomas. Immunohistochemical analysis of these tumors confirms that, although they primarily secrete insulin, they also produce other hormones, including glucagon, somatostatin, pancreatic polypeptide, and gastrin. Using routine histologic criteria of malignancy, many of these tumors appear benign, however, their biologic behavior is aggressive, with 50% of affected dogs having metastatic disease at the time of diagnosis. The regional lymph nodes and liver are the most common sites of metastasis. The normal regulatory system of insulin production is based on glucose concentrations within the pancreatic beta cells. When glucose concentrations are less than 80 mg/dL in a normal animal, insulin secretion is inhibited. Functional beta cell tumors secrete insulin in excessive amounts resulting in hypoglycemia.

Surgery is essential for appropriate management of dogs with insulinoma.

Insulinomas are most commonly reported in medium- to large-breed dogs with a mean age of 9 to 10 years. Dogs typically present with clinical signs related to hypoglycemia, including seizures, weakness, col-

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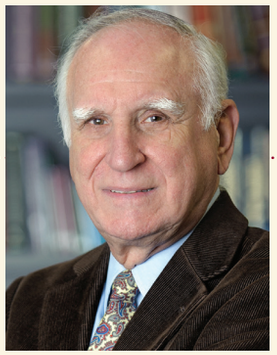
A Note from the Editor



LIVS celebrates its twentieth year serving the veterinary community locally and in the area of the surrounding states. It has earned an international reputation with its staff lecturing to professionals worldwide; currently, our chief of staff, Dr. Dominic Marino is in Guangzhou, Shanghai and Beijing China presenting a series of talks to Chinese surgeons. Practitioner referrals have allowed LIVS to pioneer novel diagnostics and treatments and it is with great pride that it continues to offer these services in support of the veterinary community.

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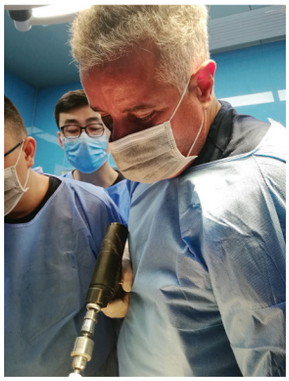

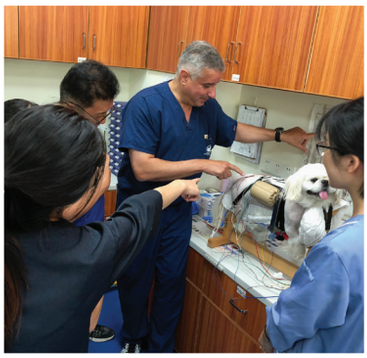

Canine Insulinomas

➤ *Continued from Front Cover*

lapse, ataxia, and mental dullness. Signs are often triggered by excitement, exercise, or fasting. Dogs may experience a peripheral polyneuropathy, with secondary paraparesis or tetraparesis and facial nerve dysfunction. Occasionally esophageal motility and anal tone may be decreased.

Routine biochemical findings in dogs with insulinoma are not specific but are supportive. Hypoglycemia may be a consistent or an intermittent finding on repeated blood glucose measurements. Specific analysis for insulinoma includes measurement of serum insulin concentrations during a period of documented hypoglycemia (blood glucose level < 60 mg/dL). Increased or inappropriately high insulin concentration (normal [5 to 26 µU/ mL]) with concurrent hypoglycemia is highly supportive of the diagnosis. Decreased fructosamine concentration may also support the diagnosis. On cytology, beta cell tumors lack the pink zymogen granules commonly seen in the cytoplasm of pancreatic exocrine cells.

Thoracic and abdominal radiographs are normal in most affected dogs. Ultrasonography is the most common modality used for the diagnosis of insulinoma (**Figure 1**) and evaluation for metastatic disease. In dogs with confirmed insulinoma, a pancreatic mass and abdominal metastasis were identified on abdominal ultrasonography in 56% and 19% of cases. With B-mode ultrasonography, insulinomas appear hypoechoic, and with contrast-enhanced ultrasonography, insulinomas appear uniformly hypervascular. Although CT reportedly had increased sensitivity for detection of pancreatic insulinoma, false-positive results in screening for metastases are common.

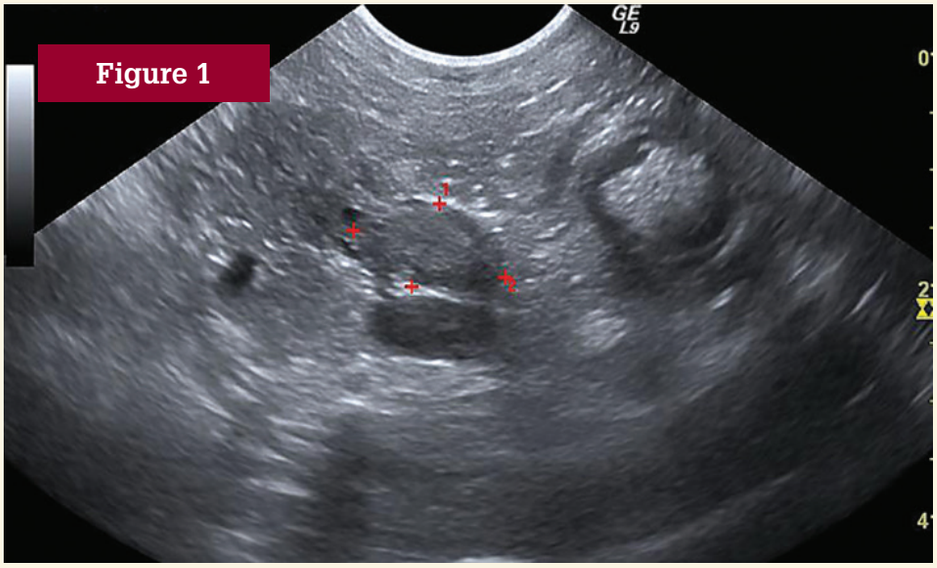

Figure 1

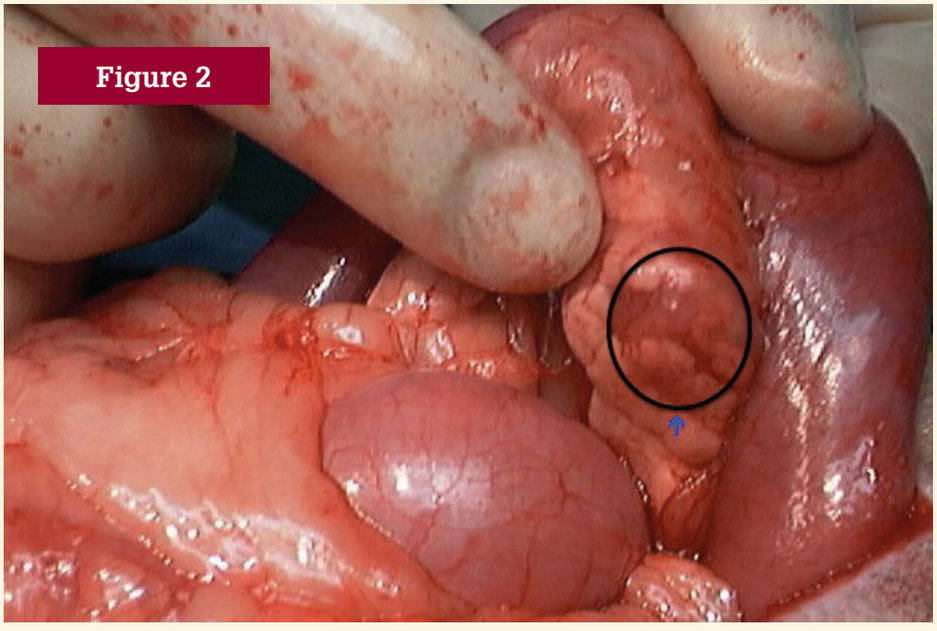

Figure 2

Treatment of hypoglycemia includes intravenous bolus administration of dextrose. If the dog's mental status improves after a bolus, frequent meals can be offered to maintain euglycemia. If illness or other factors prevent oral consumption of complex carbohydrates and protein, a constant rate infusion of 2.5% to 5% dextrose can be provided intravenously. Blood glucose concentrations should be monitored frequently during treatment. In some dogs with insulinomas, a bolus of intravenous glucose can result in further stimulation of insulin production, worsening the hypoglycemia. In those patients, treatment with glucagon may be required to balance the hyperinsulinemia.

Dogs should be stabilized before surgery by feeding frequent small meals and by limiting exercise and excitement. Glucocorticoid therapy, which increases hepatic glucose production and decreases cellular glucose uptake, may be instituted to facilitate normalization of blood glucose concentrations before surgery. Preoperative fasting may be contraindicated because of hypoglycemia; instead, a small meal of canned food should be fed 2 to 3 hours before surgery.

Surgery is essential for appropriate management of dogs with insulinoma. Surgery is not usually curative because of the frequency of metastatic disease, but reducing the amount of neoplastic tissue will improve response to medical management and survival time. Surgical exploration facilitates confirmation of the diagnosis, assists in staging of the disease, and allows resection of as much gross disease as possible. In approximately 80% of dogs, a solitary 0.5 to 4 cm nodule is evident within the pancreas. Tumors may be located in any area of the pancreas, and on gentle palpation the tumor usually feels more firm than the remaining pancreas (**Figure 2**). A partial pancreatectomy is performed to remove the primary pancreatic tumor. We make use of a vessel sealing device called a ligasure for partial pancreatectomy in dogs with insulinoma. This tool is associated with shorter surgical and hospital stays, as compared with conventional suture fracture technique, and does not result in clinical signs of pancreatitis. Regional lymph nodes and the liver are biopsied to determine the accurate stage of disease. Liver metastases are fre-

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Canine Insulinomas

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quently identified as pale nodules throughout the liver parenchyma.

If the primary tumor cannot be identified, a diluted solution of sterile methylene blue can be given intravenously to aid in identification of the islet cells. Maximal staining is achieved within approximately 30 minutes. Heinz body anemia has been reported in dogs receiving methylene blue. If the tumor still cannot be identified, multiple pancreatic biopsies can be taken in an attempt to provide a definitive diagnosis and identify tumor location for subsequent surgery.

Postoperative blood glucose concentrations must be monitored closely. In some dogs, transient hyperglycemia may occur, requiring administration of insulin. In others, hypoglycemia persists because of a continued presence of pancreatic or metastatic nodules. Further treatment of insulinoma is based on whether or not euglycemia is reached after mass excision. Pancreatitis may develop after manipulation of the pancreas and in some cases may be life threatening. If clinical signs of pancreatitis occur, aggressive management must be instituted.

Medical management of hypoglycemia is directed at either killing the neoplastic cells or treating hypoglycemia. Streptozocin, a nitrosourea antibiotic, selectively destroys beta cells in the pancreas or at metastatic sites. Other noncytotoxic drugs used to control hypoglycemia include glucocorticoids, diazoxide, and octreotide. Diazoxide is a benzothiadiazine derivative that inhibits insulin secretion, stimulates hepatic gluconeogenesis and glycogenolysis, and inhibits use of glucose. Octreotide, a long-acting synthetic somatostatin analogue, binds to somatostatin receptors and inhibits insulin synthesis and secretion. Its effects are short lived, however, with insulin suppression lasting only 3 to 4 hours.

The prognosis for patients with insulinoma varies, depending on the clinical stage of disease at the time of diagnosis and surgery.

The prognosis for patients with insulinoma varies, depending on the clinical stage of disease at the time of diagnosis and surgery. Reports indicate that dogs that had undergone surgery and subsequent medical management were more likely to become euglycemic, remain euglycemic for longer periods of time, and have longer survival times than dogs that did not undergo surgery. Even if complete excision of gross disease cannot be achieved, any reduction in tumor burden may improve the success of medical management. Dogs with no evidence of metastases at the time of surgery may be euglycemic for about 14 months, dogs with metastatic disease at the time of surgery may be euglycemic for about 2.5 months. The median survival time for dogs without detectable metastatic disease can be around 18 months and for dogs with metastatic disease around 7 to 9 months. Prognosis is poor when tumors were ≥ 2 cm, metastasized to both liver and local lymph nodes, or have a Ki67 index > 2.5%. ❑

A Note From The Editor

➤ *Continued from Page 3*

Our local news is a bit novel as coyotes have been spotted in Searingtown, and an interest in raccoon dogs, a.k.a. Nyctereutes procyonoides,(neither a raccoon nor a dog, but it does belong to the canid family), has increased. Upstate in Niagra county, distemper has been uncovered in raccoons and is easily spread to dogs. Being wary of pet/raccoon encounters is prudent. Up to now, raccoon dogs in the US are only found in the Atlanta zoo. Unfortunately, the animals are inhumanely bred for their fur, which is used in fur coats and calligraphy brushes. Back in 2014, Kohl's came under fire for advertising faux fur on jackets that actually contained real raccoon dog fur. A similar thing happened in 2006 when Macy's sold jackets made from raccoon dog fur. The lesson being that just because something's marked "faux fur" doesn't necessarily mean it's not real animal fur. Most of the fur comes from China; raccoon dogs originated in Asia.

The first domesticated dogs of North America arrived with people from Asia over the same Bering land bridge used much earlier by humans and they thrived for thousands of years, but mostly vanished after contact with Europeans. They were similar to Arctic dogs like Siberian huskies or Alaskan malamutes.

July has been a hot month and the US has been the seat of raging wildfires in the West and in Europe as well. Uncontrolled fires in Greece especially, have caused dozens of deaths. Floods in some areas and fires in others constantly remind us of the power of nature.

The warm weather brings with it the danger of pets, and children too, being left in cars. Quite dangerous for even a few moments as temperatures reach unbearable levels in minutes, as high as 160 degrees in 10 minutes when the temperature outside is 90. Irreparable damage, even death can occur in 10 to 20 minutes in those instances. A medical worker recently "forgot" her child in her car when going to work and the child was dead at shift's end when she was discovered. Pet owners and parents too, must be aware of this danger. Law enforcement officials are permitted to break windows to rescue pets or children when found inside locked vehicles. If civilians come upon this situation, they should call the police first, and check to see if the car is unlocked before breaking the glass.

Every month, Dr. Curtis Dewey, associate professor and section head of Neurology/Neurosurgery at the College of Veterinary Medicine at Cornell is here at LIVS regularly for consultation as is our animal behaviorist, Dr. Sabrina Poggiagliolmi. Appointments can be made at 516 501-1700.

As before we welcome all comments, please submit them to lmarino@livs.org

Leonard J. Marino, MD, FAAP, LVT

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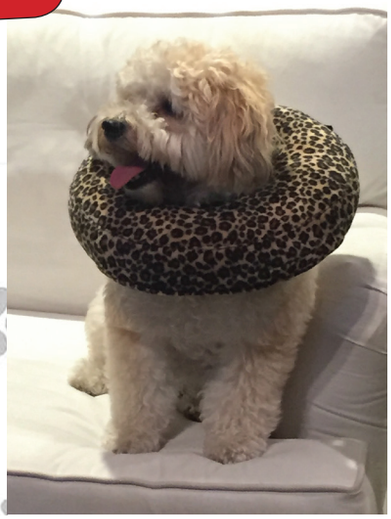

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Anterior Lens Luxations In A Dog

John S. Sapienza, DVM, Diplomate, ACVO

The crystalline lens is held in place by suspensory ligaments called the zonules. Any disruption to these zonules, such as an inherited zonular degeneration, trauma or disruption from buphthalmos, can lead to a lens subluxation or even complete luxation. If the lens is luxated into the posterior segment of the eye, specifically in the vitreous cavity, urgent medical or surgical intervention is usually not necessary, however, if the lens is luxated in the anterior chamber, marked impediment to the outflow of aqueous humor can occur, leading to an acute glaucomatous crisis. Hereditary or genetic lens subluxations/luxations are extremely common in the terrier breeds (Tibetan Terrier, Wirehaired Fox Terrier, Sealyham, Jack Russell Terrier, Miniature Bull Terrier and West Highland White Terrier) as well as in older small breed dogs (Poodles, Maltese, Bichon Frise, Yorkshire). Primary lens luxations have also been reported in the Border Collie. In our population of Long Island dogs, the incidence of primary lens luxations is higher in the Jack Russell Terrier breed. In fact, if a Jack Russell Terrier presents with a lens luxation in one eye, the second eye typically has a lens subluxation and is thus predisposed to develop a lens luxation in the near future. Typically, strands of vitreous are observed in the anterior chamber or through the pupil with a lens subluxation.

If a canine patient presents acutely with an anterior lens luxation (ALL), secondary glaucoma is often the clinical outcome. Classical clinical signs of an ALL can include an acutely painful eye, blepharospasm, and a cloudy cornea. At times, the corneal edema would be so dense as to obstruct a clear view into the eye. Suspicion of an ALL, especially in the typical Terrier breed, is imperative to successful and speedy management of these cases. One practice tip that I can share is to use one's cobalt blue light to illuminate the eye in cases of a suspected ALL. The lens will actually be evident as a blue structure in the anterior chamber! In cases of an ALL, the intraocular pressure frequently will be greatly elevated. If one looks closely into the eye, the periphery of the luxated lens is often readily visible in the shallow anterior chamber. **Figure 1**. In cases of a lens subluxation, vitreous can be seen as wisps and strands in the anterior chamber or through the pupil, and the iris or the lens may be observed to shake as the eye moves (iridodonesis and phacododonesis, respectively). **Figure 2**.

Rapid diagnosis and quick surgical intervention is the key to successful therapy of an anteriorly luxated lens.

Rapid diagnosis and quick surgical intervention is the key to successful therapy of an anteriorly luxated lens. An ALL is an ocular emergency! If glaucoma is present, time is of the essence. Prompt referral to your regional ophthalmologist is necessary. Once our specialist ophthalmic team receives the case, we would institute an intravenous mannitol

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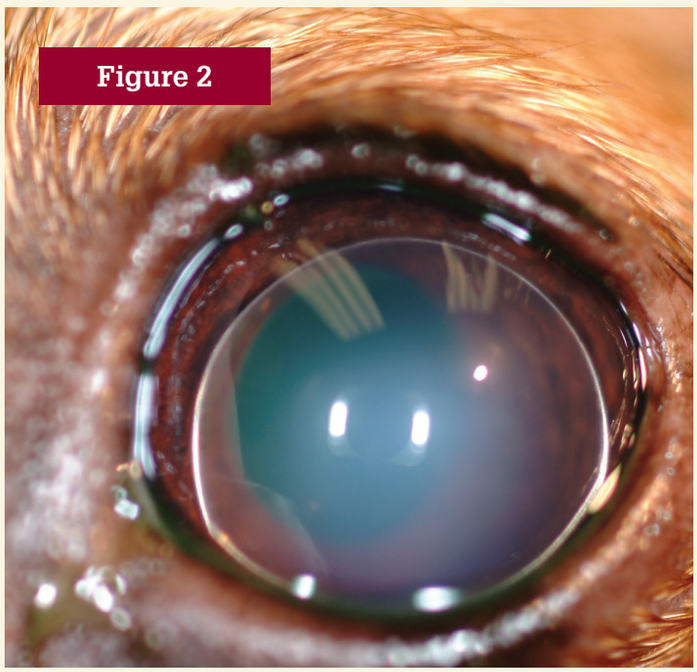
Figure 1

Figure 2



Canine Insulinomas

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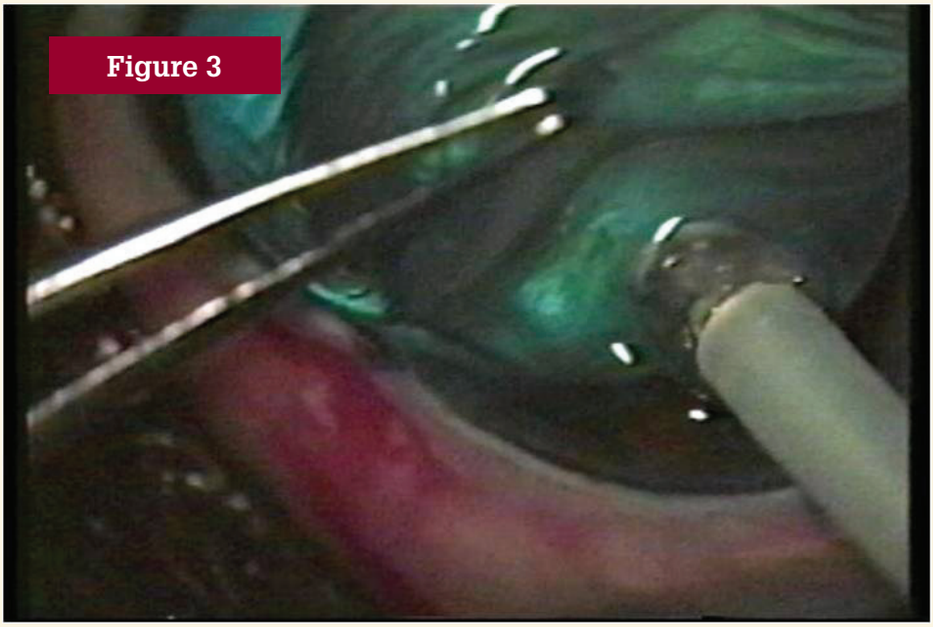
drip, and plan to take the patient to surgery shortly thereafter to remove the lens. One should avoid the use of pilocarpine or prostaglandin analogues in the face of an ALL, as these drugs will further trap the anteriorly luxated lens into the anterior chamber and aggravate the glaucoma crisis. Under general anesthesia, a planned intracapsular lens extraction would be performed. The luxated lens is typically removed through a large dorsal clear cornea incision with the aid of a cryophake (a probe which withdraws the lens via cryoadhesion). **Figure 3**. Additional consideration at the time of lens extraction would be to perform a sulcus suturing of an intraocular lens.

The keys to success with anterior lens luxations are: suspicion of an ALL in the typical breed (be wary in Jack Russell Terriers), rapid diagnosis, intraocular pressure control, prompt medical therapy, and accurate surgical intervention. ❑



LENS LUXATIONS:

- If anterior, recommend immediate referral to the ophthalmologist.
- If the lens is posteriorly luxated, urgency is less so than with an ALL, but these posteriorly luxated cases should be referred in a timely fashion.
- If glaucoma is present as well as potential for vision, an intracapsular lens extraction will be performed with or without an endolaser therapy.
- If glaucoma is present in an irreversibly blind eye (typically, in patients where the glaucoma has been present for over 2-3 days with no light perception), an intrascleral prosthesis or an enucleation may be advised.

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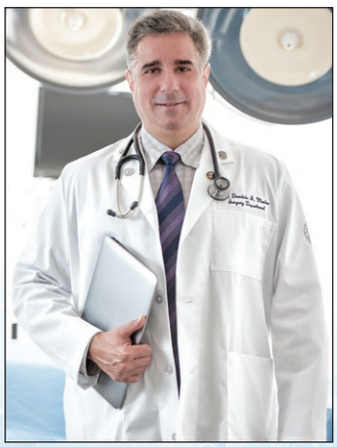

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