

A Review of Infectious Liver Diseases

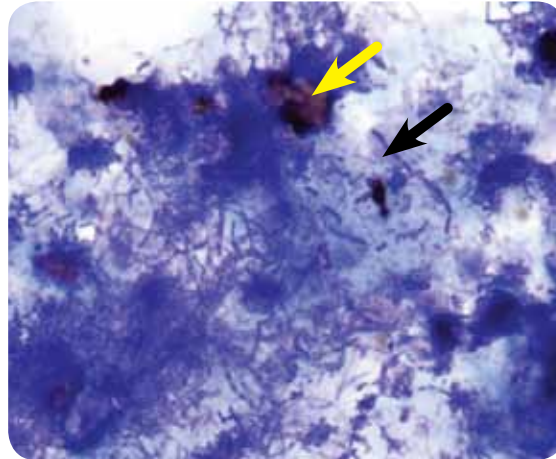


By Shawn Kearns,
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The liver plays a major role in guarding against infections due to its central position between the enteric and systemic circulation. Its location, dual blood supply, and extensive sinusoidal system also make the liver susceptible to disseminated infectious organisms when normal defense mechanisms fail. Clinical signs, biochemical and hematologic parameters, and diagnostic are often non-specific and may include fever, hepatosplenomegaly, lethargy, jaundice, vomiting, diarrhea, weight loss, polyuria/polydipsia, and abdominal pain. Table 1 (see page 5) shows a list of organisms reported to affect the liver primarily or secondarily, but this review will focus on those most commonly seen (in general) and those seen in

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the New England region. Under various conditions, alimentary flora circulates to the liver and, in health, these bacteria are extracted by Kupffer cells, killed by neutrophils or excreted in bile. When portal flow is compromised, changes in this sinusoidal flow may decrease the effectiveness of phagocytosis. With altered portal circulation, bowel disease, cholestasis, immunosuppression, and altered gut motility there may be unchecked bacterial access to the liver, leading to bacterial hepatitis or cholangiohepatitis. Common isolates include *Escherichia coli*, *Enterococcus* spp., *Bacteroides* spp., *Streptococcus* spp., and *Clostridium* spp. A combination of liver and gallbladder samples (Figure 1) may increase the likelihood of identifying the offending organism(s), and surgical or laparoscopic biopsies may be



➤ **Figure 1:** Fine needle aspirate and cytology from the gallbladder of a cat with cholangiohepatitis. The aspirate consists predominantly of bacteria of mixed type. The bacteria are frequently present in chains (black arrow). Also, note dark brown-staining amorphous material (bile pigment — yellow arrow). The finding of bacteria in cytologic specimens of bile is considered abnormal. The following organisms were cultured from the bile: *E. coli*, *Streptococcus pneumoniae*, an anaerobic bacterial rod, *Prevotella oralis*, and a gram-positive rod that could not be classified. *Courtesy of the Pathology Department, Angell Animal Medical Center, Boston, MA.*

more rewarding for culture growth compared to aspirates. Broad-spectrum antibiotics for common enteric isolates are often started pending specific culture results. Less common bacterial liver isolates include *Bartonella* spp. (*Bartonella henselae* and *Bartonella clarridgeiae*), *Helicobacter* sp, *Francisella tularensis*, *Clostridium piliforme*, and *Rhodococcus* sp.

Leptospirosis is one of the most common non-enteric bacterial infections seen within the liver of the dog. Spread and replication occur in many tissues, including the liver, but the organism tends to persist in the kidney and can be shed for weeks to months after infection. Certain serovars are more often associated with liver involvement (icterohaemorrhagiae and Pomona). Young dogs (< 6 months) may develop signs of hepatic dysfunction more frequently in disease outbreaks.

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Don't Amputate That Ear! Reconstructive Surgical Options for Defects of the Pinna



By Michael Pavletic,
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Many veterinarians are unaware of the reconstructive surgical options available for defects of the pinna secondary to trauma and tumor resection. Amputation of the pinna in a number of cases can be avoided. The available reconstructive surgical options for the management of pinnal defects depends upon the size of the lesion, its location on the pinna, and the anatomic conformation based on the breed and species.



➤ Figure 1: Mast cell tumor (Grade II) involving the inner pinna.



➤ Figure 2: Wide resection of the tumor, including the underlying pinnal cartilage.

From a practical standpoint, amputation of the terminal “third” of the pinna is a realistic option, based on the intimate relationship between the pinnal cartilage and the overlying skin surfaces. For those cases with extensive neoplasia extending into the lower pinna, complete amputation of the pinna is usually indicated. It is interesting to note, however, that the lower two thirds of the pinna have a different anatomic configuration to the terminal ear region. The outer pinnal skin reflecting off the dorsum of the head is mobile and comparatively free of the pinnal cartilage attachment. The skin

then transitions into a progressively closer association with the cartilage as it ascends to the terminal third of the pinna. This permits the surgeon to consider simple skin flap options for closure of defects in the lower “half” of the ear, both on the inner and outer aspects of the pinna. Distance, however, is relative to the length of the ear. For example, short ears on a dog may allow a skin flap to extend to the tip of the pinna.

Transposition flaps are the most effective local flap option to close surgical defects after removal of the diseased skin and underlying cartilage layer. Simple skin advancement may suffice for lower pinnal defects involving the base of the ear. The available skin around the base of the ear and vertical ear canal regions serve as ideal donor areas for pedicle graft development. The author has also used transposition flaps to cover large areas of denuded pinna secondary to trauma. In cases of extensive skin loss involving the outer pinnal surface, the author has used the Caudal Auricular Axial Pattern Flap to resurface the entire outer pinnal surface.

For more information about reconstructive surgical options, or if you have any questions regarding any challenging cases, Dr. Pavletic welcomes your inquiries. Dr. Pavletic is Director of Surgery at Angell, and the author of Wiley-Blackwell's *2010 Atlas of Small Animal Wound Management and Reconstructive Surgery, Third Edition*. You can reach Dr. Pavletic by calling 617 541-5048 or e-mailing mpavletic@angell.org. For information about Angell's Surgery service, please visit angell.org/surgery. ■



➤ Figure 3: Closure using a transposition flap developed from the adjacent skin.



➤ Figure 4: View of the patient's head and pinna postoperatively. The patient made a complete recovery. Surgical margins were achieved in this case.



What's New in Glaucoma Management?



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The biggest change in our management of glaucoma this year has been the advent of a generic equivalent to Xalatan®¹ 0.005% latanoprost.² This has resulted in a significant price drop (from \$80–90 per 2.5ml bottle to less than \$15), making latanoprost far cheaper than dorzolamide and on par with timolol. While we expect this to make glaucoma management more affordable for many clients, we have noticed a significant increase in the number of cases started on latanoprost prior to referral. In light of this new generic topical prostaglandin on the market, some new caveats must be considered when choosing glaucoma drugs in practice.

To the authors' knowledge, there have been no clinical trials in dogs comparing the efficacy of Xalatan to its generic equivalent. In humans, such a study was performed in 2007, comparing Xalatan to its generic equivalent in India.³ The results showed a statistically significant difference between the two drugs, with Xalatan lowering intraocular pressure (IOP) more than latanoprost, and a greater incidence of irritation by the generic formulation. However, the IOP difference may not have been clinically significant. It is also worth noting that the generic available in the United States is not likely the same product as the Indian version.

In our clinical experience with patients who were switched from Xalatan to generic latanoprost at Angell Animal Medical Center, we have yet to see any adverse effects or treatment failures, but one must keep this potential difference in mind when evaluating therapeutic response.

Latanoprost, similar to other prostaglandin analogues such as travoprost and bimatoprost, is a PGF_{2α} prostaglandin analogue that increases aqueous humor outflow from the canine eye by both the unconventional, or uveoscleral, outflow pathway and the conventional iridocorneal angle aqueous outflow, in part by causing remodeling and opening of the outflow pathways. It also induces miosis, which may be profound in some cases (Figure 1). Increased scleral injection is also noted with latanoprost use in some canine patients. Latanoprost is typically more potent and quicker-acting than carbonic anhydrase inhibitors (CAIs) or beta blockers, such as dorzolamide or timolol, respectively, and is an excellent choice in emergency treatment of primary glaucoma, as well as for maintenance therapy of primary glaucoma that is inadequately or not at all responsive to CAIs or beta blockers. In cases that show good response to CAIs and/or beta blockers

(typically when the IOP is 20mmHg or less on medication), we recommend withholding latanoprost. Assuming that IOP can otherwise be controlled, latanoprost can worsen vision since it induces miosis and, over time or at high frequencies, can induce low-grade uveitis that can lead to posterior synechia or even glaucoma exacerbation. Having said that, we do manage some primary glaucoma cases with latanoprost as a sole agent, since it may have better client compliance as a once- to twice-daily use (by contrast, dorzolamide is given every eight hours).

Consultation with a veterinary ophthalmologist is recommended if you are considering managing glaucoma in a patient, either solely with latanoprost or in conjunction with other glaucoma eye drops: there are significant and potentially costly pitfalls to using latanoprost in the wrong situation. Latanoprost is generally contraindicated in glaucoma secondary to anterior lens luxations, advanced anterior vitreal degeneration present in the anterior chamber, and some partial anterior subluxations. Any pupillary constriction can further entrap the lens and vitreous anteriorly, leading to pupillary block glaucoma. Since latanoprost is a PGF₂ analogue, a mediator of inflammation, extreme caution must be used when considering it in the treatment of glaucoma secondary



➤ **Figure 1:**
Latanoprost-induced
miosis in a dog.

to uveitis, or even primary glaucoma with a significant uveitic component. Exacerbation of uveitis has the potential to worsen glaucoma, for example by inflammation of the iris leading to occlusion of the filtration angle, or from rapid development of posterior synechia, fibrin, hyphema, and hypopyon. If the glaucoma is not responsive to CAIs or beta blockers, and uveitis is present, judicious latanoprost use

along with anti-inflammatories may be beneficial. However, it is best to leave that decision to the veterinary ophthalmologist.

In summary, although the cheaper availability of latanoprost opens it to far more widespread use, caution must still be exercised. A complete ophthalmic examination to determine the etiology, primary or secondary, of the elevated IOP is vital. For ongoing maintenance therapy of glaucoma, it may be too potent for many cases, and may be more beneficial as a reserve drug when others begin to fail.

For more information about Angell's Ophthalmology service, please visit angell.org/eyes. Drs. Coster and Biros are available for consultations or referrals at **617 541-5095**, or e-mail ophthalmology@angell.org. ■



1. Xalatan, Pfizer Inc, New York, NY
2. e. g., Latanoprost 0.005%, Greenstone LLC, Peapack, NJ
3. Narayanaswamy A, Neog A, Baskaran M, George R, Lingam V, Desai C, Rajadhyaksha V. A randomized, crossover, open label pilot study to evaluate the efficacy and safety of Xalatan® in comparison with generic Latanoprost (Latanoprost) in subjects with primary open angle glaucoma or ocular hypertension. *Indian J Ophthalmol* 2007; 55:127–131.

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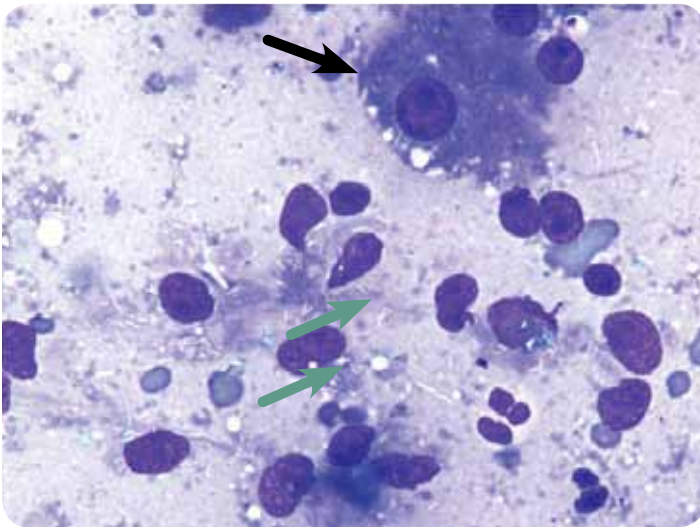
Diagnosis is usually made based on clinical signs and serologic titers; however, urine polymerase chain reaction (PCR) performed prior to treatment may increase testing sensitivity, given vaccinal interference and delayed seroconversion in the acute phase. Penicillins (acute phase) and doxycycline (acute and carrier states) are the treatment of choice.

Non-tuberculous mycobacteria are most often implicated in disseminated disease in cats and occasionally in dogs. Certain breeds appear more susceptible, including Basset hounds, Miniature schnauzers, Siamese, and Abyssinians. Dogs will often have extensive granulomatous disease of the intestine, spleen, liver, and mesenteric lymph node. Animals undergoing immunosuppression with drugs inhibiting cell-mediated immunity may be at risk for disseminated disease. Routine stains (negative images of bacteria, Figure 2), acid-fast stains, PCR, and culture may aid in a diagnosis. Even with combination therapy, treatment may not be rewarding, especially with disseminated disease.

in German shepherds, non-shepherd breeds, and cats. Neurologic deficits, spinal column pain, urinary system disorders, and respiratory pathology are the primary clinical signs for which patients will present. With treatment of disseminated fungal disease, clinical signs may resolve but relapses occur, and those severely ill tend to have a poor prognosis.

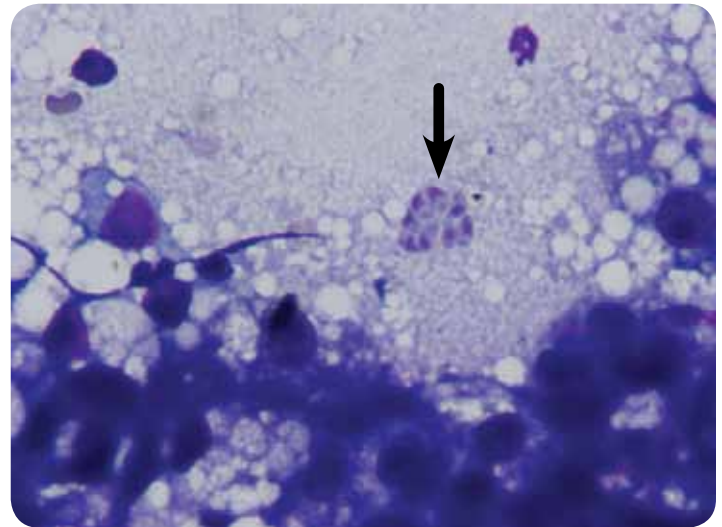
Non-tuberculous mycobacteria are most often implicated in disseminated disease in cats and occasionally in dogs. Certain breeds appear more susceptible, including Basset hounds, Miniature schnauzers, Siamese, and Abyssinians.

Toxoplasmosa gondii is an obligate, intracellular coccidian parasite that infects almost all warm-blooded animals. The tachyzoites can form cysts in the CNS, muscle, and visceral organs. Liver and



➤ Figure 2: *Mycobacterium* in the liver of a cat. The aspirate consists of hepatocytes (black arrow) admixed with inflammatory cells that include macrophages and fewer small lymphocytes, plasma cells, and neutrophils. Numerous extracellular and intracellular (within macrophages) negative images of bacterial rods are seen (green arrows).

Courtesy of the Pathology Department, Angell Animal Medical Center, Boston, MA.



➤ Figure 3: *Toxoplasma gondii* tachyzoites from a liver aspirate in a cat. The patient presented with rapidly progressing signs associated with liver and pulmonary disease.

Courtesy of the Pathology Department, Angell Animal Medical Center, Boston, MA.

Dissemination of fungal organisms, like most other diseases, is via the hemolymphatic system. *Aspergillus*, a ubiquitous fungus with broad geographic range, is most often associated with rhinitis; however, several reports have documented systemic infections

lung involvement tend to lead to death in a shorter period of time than other organ involvement. Tachyzoites may be detected on cytology of various organs (Figure 3) and body fluids, but diagnosis is most often based on clinical signs, serology (IgG, IgM), and response to treatment. Treatment of choice is clindamycin.

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Other than feline infectious peritonitis (FIP), viral diseases affecting the liver in dogs and cats are uncommon. With FIP, affected felines develop signs related to lesions in the target organ (kidney, liver, CNS, intestine) or due to fluid redistribution. Hyperbilirubinemia is most often due to vasculitis in the liver. Diagnosis is definitive only with histopathology but supported by history, physical exam, and laboratory findings. A new PCR test may also prove useful in the diagnosis of FIP, and multiple samples (fluid, blood, tissue) may increase likelihood of a diagnosis. Treatment is generally unrewarding. Conflicting information exists on the usefulness of feline recombinant interferon; however, this may benefit a subpopulation of cats with FIP.

Rickettsial organisms (*Ehrlichia* sp., *Rickettsia rickettsii*, and *Borrelia*) can infect either hepatocytes or endothelial cells. Rocky Mountain Spotted Fever, being vasculotropic in nature, is more commonly associated with increases in elevated liver enzymes compared to other tickborne diseases. With treatment, values often return to normal over the course of several weeks.

There are many infectious diseases that ultimately affect the liver. Few, however, have primary tropism for hepatic tissue. Testing should be directed based on signage, geographic location, and primary presenting complaint. Cytology and/or histopathology of the liver will most often give a definitive diagnosis when there is liver involvement. The prognosis is guarded, with many disseminated infections.

To contact Dr. Kearns about infectious liver diseases or other topics, please call 617 522-7282 or e-mail her at skearns@angell.org. For more information about Angell's Internal Medicine service, please visit angell.org/internalmedicine. Angell's internists are available for consultation via phone 617 522-7282 or e-mail internalmedicine@angell.org. ■



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Table I: Infectious Organisms Affecting the Liver in Dogs and Cats

Bacterial Diseases

Numerous aerobic and anaerobic enteric and non-enteric bacteria*

Leptospirosis*

Disseminated Fungal Infections (*Mycobacterium)

Histoplasma capsulatum

Coccidioides immitis

Blastomycosis dermatitides

Aspergillus sp.*

Cryptococcus sp.

Sporothrix schenckii

Prototheca zopfii

Disseminated Protozoal Infections

*Toxoplasma gondii***

Leishmania sp

Hepatozoon canis

Hepatozoon americanum

Encephalitozoon cuniculi

Cytauxzoon felis

Neospora caninum

Sarcocystis canis

Viral Disease

Feline infectious peritonitis*

Infectious canine hepatitis

Canine acidophil hepatitis (Great Britain)

Canine herpes virus

Feline leukemia

Rickettsial Disease

*Rickettsia rickettsii**

Ehrlichia sp.

Borrelia burgdorferi

Parasitic Disease

Opistorchus

Metorchis

Platynosomum concinnum

*Indicates the more commonly seen diseases or those more common to New England

Intra-Testicular Nerve Blocks: An Easy and Inexpensive Way to Augment Post-Castration Analgesia



By Lisa Moses,
VMD, DACVIM, CVMA
painmedicine@angell.org



In support of our mission, we strongly advocate spaying and neutering. Angell's Pain Medicine Service keeps our anesthesia and analgesia protocols updated and as cost-efficient as possible. By adding intra-testicular blocks to our cat and dog neuters, we can increase analgesia significantly without much effect on cost, efficiency, or risk.

If you are asking "why bother" adding another step to an already quick surgery in most practices, remember that good pain control prevents central sensitization in the nervous system. This is our best chance to prevent or dampen chronic pain syndromes later in life for our patients. This technique can also cut down on the amount of anesthesia and analgesia drugs used peri-operatively, thereby reducing risk of side effects, long recovery times, and maybe even overall cost. Besides, isn't better pain control our goal for our patients?

This block can be done on virtually any patient undergoing routine castration. This technique is particularly helpful in a patient that has higher risk for general anesthesia complications (like those with heart disease) or older patients who are likely to be more reactive during surgery and may have more post-operative pain.

Materials required are two 1/2-inch 25g and/or 22g needles, 2% lidocaine and/or 5% bupivacaine, morphine or buprenorphine for injection. Other opioid and α -2 agonists have also been described for use. As with any locoregional nerve block, the choice of drugs influences onset and duration of action. If you perform castrations very quickly after prepping your patient, then you may want to use lidocaine in your mixture for fastest onset of action, or mix it with bupivacaine and/or an opioid for longer duration. When lidocaine and bupivacaine are mixed, the overall duration of effect is probably less than for bupivacaine alone, but you do get onset a few minutes earlier. Adding an opioid to the mixture will add hours of duration to your block. We generally use 1 mg/kg of 5%

bupivacaine and 0.075 mg/kg morphine. You could also add 0.5-1 mg/kg of lidocaine. The volume is more than enough in either case.

To perform the block, first surgically prep as you normally would. The block should be done under conditions as aseptic as possible with sterile gloves. Isolate and stabilize one testicle, then insert the needle from the caudal pole along the long axis of the testicle. The tip of the needle should be in the middle of the testicle or in the cranial 1/3. Aspirate to make sure you have not hit a vessel on your way in. If not, slowly inject until the testicle feels turgid and backpressure is evident. Then carefully remove the needle without injecting any further or keeping a vacuum on the syringe. Repeat on the other testicle. You will probably have extra solution left; this can be used to do a line block in the area of your pre-scrotal incision on a dog. The whole thing should take you less than two minutes.



➤ Dr. Moses administers an intra-testicular nerve block.

Complications have been rarely reported with this block, but if you look it up on VIN, you will see that some veterinarians have seen some post-op bleeding or hematoma formation. We have not seen this happen at Angell, but if you puncture a vessel in the right place, it probably easily can.

For another description or to see a short and very instructive video, search for "intratesticular block" on Dr. Bob Stein's excellent web site: VASG.org.

For more information, to make a Pain Medicine referral, or to discuss Angell's Telemedicine program and other opportunities for Pain Medicine consulting/training by phone or at your practice, please contact Dr. Lisa Moses at 617 541-5140 or painmedicine@angell.org or visit angell.org/painmedicine. ■



CE SEMINAR



Upcoming Angell CE Seminar: Re-Emergence of Infectious Diseases in New England

Sunday, November 6, 2011
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Guest Speakers:

- **Peggy Barr**, DVM, PhD, Professor of Virology and Immunology, Western University
- **Lesley Geraldine King**, MVB, MRCVS, DACVIM, DAVECC, Director, Intensive Care Unit, Veterinary Hospital of the University of Pennsylvania, Department of Clinical Studies – Philadelphia School of Veterinary Medicine
- **Frank Muggia**, BA, JD, Member of Harris Beach PLLC, Attorneys-at-Law, Approved consultant by the American Animal Hospital Association, Member of the American Veterinary Medical Law Association

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For additional information, please contact Eleanor Cousino, Angell Referral Coordinator, at 617 522-5011, or by fax at 617 989-1635.



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We encourage you to e-mail Angell's specialists with questions. We hope you will use Angell as a resource, and we look forward to working with you as we continue our legacy of providing compassion and care for animals.

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