Stabilizing the Trauma Patient Prior to Referral

Andrea Sundholm, DVM, DACVS-SA

DoveLewis Annual Conference Speaker Notes

The emphasis of this discussion will be on addressing common injuries sustained during trauma that may require intensive or surgical intervention. Briefly, the initial assessment and stabilization will be reviewed along with the basics of trauma screening and starting treatment. The remainder of the discussion will focus on diagnosis and treatment of pneumothorax, hemoabdomen, wounds and fractures.

The initial assessment of your patient should start with identifying the most life threatening problems first. Performing a complete and thorough physical exam will help identify issues with their airway, ventilation and circulation. Observing their breathing pattern and performing thoracic auscultation can possibly clue you in to a pneumothorax. Assessing their pulse rate and quality, mucous membrane color and capillary refill time will help you decide if your patient is in shock. Complete full vitals and repeat these vital parameters in order to watch for trends. Once you have made an initial assessment, provide pain management. Given the patient recently had trauma, a pure mu agonist is recommended such as hydromorphone, methadone or fentanyl. Until cardiovascular stability is confirmed and maintained, wait on giving non-steroid anti-inflammatories. Steroids are generally contraindicated in trauma patients and should be avoided. Depending on your patients' clinical findings, fluid therapy may be necessary to address hypovolemic shock. The current recommendations are to give increments of a shock bolus and frequently monitor perfusion parameters.

Trauma screening involves obtaining thoracic radiographs, abdominal imaging and completing bloodwork. Thoracic radiographs should be assessed for evidence of pneumothorax, pulmonary contusions, rib fractures or diaphragmatic hernia. Depending on your equipment abdominal imaging may be radiographs or ultrasound (or both). Based on a study by Boysen et al, focused assessment with sonography for trauma has a 96% sensitivity and 100% specificity for identifying free abdominal fluid in blunt trauma cases. Additionally, this is a simple and rapid technique that can be performed by veterinary clinicians with minimal previous ultrasonographic experience. The technique involves examining four quadrants within the abdomen for evidence of free fluid the subxyphoid region, midline over the bladder and the left and right flanks. Abdominal radiographs should be evaluated for loss of serosal detail and evidence of an intact urinary bladder. Full bloodwork should be performed to complete the clinical picture of the patient. Specific parameters, such as lactate, can also be assessed help determine the potential need for blood products.

A pneumothorax occurs when airs enters the pleural space through the thoracic wall, esophagus or airways. Depending on the amount of air and other injuries to the thoracic cavity the clinical signs may be absent or severe. The restrictive breathing pattern is typical with an inspiratory dyspnea. Your physical exam may reveal diminished lung sounds, especially dorsally. The diagnosis is typically confirmed on two view thoracic radiographs. Classic signs are retraction of lung edges from the thoracic wall and elevation of cardiac silhouette from the sternum. Images should be made only upon patient stabilization because the stress associated with positioning may result in ventilatory or cardiovascular decompensation. If you believe the pneumothorax to be secondary to a penetrating wound in the thoracic cavity, immediately cover the wound to prevent the possibility of a tension pneumothorax. A thoracocentesis should be attempted in a patient with a pneumothorax. Materials can include a hypodermic needle/butterfly catheter/catheter, extension set, three way stop cock, large syringe, sterile gloves and an assistant. The chest should be clipped and prepped from about the 6-8th intercostal space. Insertion of the needle should avoid the neurovascular structures on the caudal aspect of the rib. An insertion angle of about 45° can help avoid iatrogenic trauma to the lung parenchyma. Once negative pressure is achieved, obtain post tap radiographs to subjectively assess the success of your thoracocentesis. If you are unable to achieve negative pressure, the clients should be aware of the potential for a thoracostomy tube or potentially surgery. Penetrating thoracic wounds are not automatically surgical unless signs of continuous pneumothorax, ongoing hemorrhage or suspected sepsis. Surgical exploration of wounds over the thorax should be recommended if there are rib fractures, pulmonary contusions or a pneumothorax. The retrospective study by Scheepens et al, highlights this point as rib fractures, pulmonary contusions and pneumothorax were most seen in cases where a lung lobectomy was indicated. It also showed that radiographs will not always provide a complete inventory of the visceral damage. When wounds over the thorax are explored (and pleural communication is suspected), the patient needs to have a secured airway, be anesthetized and the ability to mechanically ventilate should be available.

A hemoabdomen may not be completely obvious on your initial assessment. Signs such as abdominal distension, abdominal bruising and a fluid wave may be evident. However, our physical exam findings can have a high rate of false negatives and therefore alone is unreliable in assessing the severity of intraabdominal injury. Approximately 6-13% of animals with have intraabdominal hemorrhage after being hit by a car. Trauma to the liver, spleen and kidneys are the most common sites for hemorrhage. The diagnosis is made by coupling imaging findings (either free abdominal fluid on FAST scan or decreased serosal detail seen on abdominal imaging) and an abdominocentesis. Be aware that blood that has been in contact with the peritoneal surface for 45 minutes is free of platelets and does not clot. If clotted blood is recovered it is suggestive of inadvertent splenic or vascular penetration. To perform an abdominocentesis the patient can be standing, in lateral recumbency or dorsal recumbency. A single tap is performed on ventral midline approximately 1-3 cm caudal to the umbilicus. The site is aseptically prepped. If no fluid is obtained a four quadrant tap or an ultrasound guided tap can improve diagnostic yield.

In an attempt to slow hemorrhage, an abdominal wrap can be placed. This bandage extends from the pubis to the xyphoid. Once the patient has been stabilized, slowly cut the bandage from cranial to caudal. These bandages are contraindicated in patients with respiratory compromise, diaphragmatic hernias or head trauma. Traumatic hemoabdomens are generally medically managed and the overall survival rate with surgical or medical management is 70%. Surgical intervention is reserved for patients that cannot be stabilized despite aggressive medical therapy. In a retrospective study by Hoffberg et al, 37% of patients with pelvic fractures have evidence of intra-abdominal injury such as hemoabdomen, uroabdomen and septic abdomen. Further, dogs with sacral fractures were significantly more likely to have intra-abdominal injury, likely due to the amount of force needed to sustain this type of fracture.

Wounds are very common in the trauma patient but are usually not the most life threatening injury. Therefore, they should be filled with sterile lube and covered with a temporary bandage until the patient has been stabilized. Then, the peri-wound skin should be clipped widely and prepped with dilute chlorhexidine or dilute iodine solution. If obvious necrotic or devitalized tissue is present, surgical debridement with a scalpel blade or Metzenbaum scissors is recommended. This procedure requires aseptic technique, heavy sedation and/or general anesthesia. If the viability of tissue is questionable, leave it and assess it again at the next bandage change. Copious lavage is recommended with 8-15 psi being most effective. The fluid should be sterile and isotonic. However, tap water is perfectly acceptable and much quicker and more cost effective in wound with massive contamination. Chlorhexidine and iodine can also be added to lavage solutions for highly contaminated wounds. The type of bandage chosen to cover the wound will depend on how much support is needed and when the next bandage change is scheduled to occur. Limbs with wounds and fractures/instability should be stabilized with a splint or Robert Jones bandage. Wounds that are highly effusive should have a primary contact layer that is capable of fluid absorption, especially if the next bandage change is not within the next 24 hours. Consider the use of calcium alginate dressing or polyurethane foam. These primary wound dressings both adhere to the moist wound healing principles and can be beneficial for fluid absorption, autolytic debridement and patient comfort. A simple laceration may be covered with a Telfa pad and a modified Robert Jones bandage. If the patient requires immediate transfer due to the need for critical care, please place sterile lube in the wounds and cover with a temporary bandage.

Fractures that are easily amendable to support bandages are distal to the elbow and stifle. The bandage should support the joint above and below the fracture to maximize patient comfort and avoid a “fulcrum” effect. Bandages can also decrease or prevent edema and minimize additional trauma. Most other fractures, such as scapular, humeral, femoral and pelvic are best treated with adequate pain medications and confinement. Open fractures are classified based on the wound size and concurrent soft tissue trauma. Any wound that is overlying a fracture is assumed to have resulted in contamination of the fracture and broad spectrum antibiotics should be administered intravenously at the time of presentation. The recommendations for open fractures include copious lavage, prompt

debridement, initiation of antimicrobials and rigid fixation. Cultures are generally obtained at the time of surgery. A Robert Jones bandage is a bulky bandage that is indicated for temporary stabilization. It provides support and immobilization but is unsuitable for primary fixation. These bandages start with 1 lb 12 inch roll cotton that is placed 4-8 cm thick. Gauze is used to compress the cotton by 50% and then vetwrap is placed as the final layer. A modified Robert Jones bandage contains cast padding instead of cotton and is generally used in the post-operative period for swelling and protecting soft tissues. It is not an appropriate bandage for temporary support of fractures or dislocations. Splints can be formed with aluminum rods, preformed metal or plastic and moldable materials such as fiberglass. The material is applied after the cast padding and gauze have been placed. The preformed plastic splints can be challenging because exact fit is rare and only with excess cotton padding can the fit be improved. However, this is counterproductive to temporary fracture stabilization as the cotton will compress and therefore the support is lost. Cast padding should be minimal if a splint is being used for temporary stabilization. In the author's opinion, preformed plastic splints should not be used for primary fracture stabilization. A spica splint can be made to immobilize the shoulder or the hip and is the correct bandage for temporary stabilization of humoral or femoral fractures. The rigid splint aspect extends over the scapula or hip to dorsal midline and down to the toes. Cast padding and gauze are placed first, followed by the formed spica splint and then finished with more gauze and vetwrap. "Fanning" the fiberglass weakness the support and should be avoided.

As always, feel free to call with questions regarding your trauma patient. We are here to help!

References:

Boysen et al. Evaluation of a focused assessment with sonography for trauma protocol to detect free abdominal fluid in dogs involved in motor vehicle accidents. *J Am Vet Med Assoc* 2004;225(8):1198-204

Brockman et al. A practical approach to hemoperitoneum in the dog and cat. *Vet Clin North Am Small Anim Pract* 2000*:* 30:657-668.

Hoffberg et al. Retrospective evaluation of concurrent abdominal injuries in dogs with traumatic pelvic fractures: 83 cases (2008-2013). *J Vet Emerg Crit Care* 2016:26(2):288-94

Scheepens et al. Thoracic bite trauma in dogs: a comparison of clinical and radiological parameters with surgical results. *J Small Anim Pract* 2006;47(12):721-6

Tobias and Johnston. Veterinary Surgery: Small Animal Surgery 1st Edition.

Hepatopathy Headache: Evaluating the Asymptomatic Patient

Barbara Davis, DVM, DACVIM

DoveLewis Annual Conference Speaker Notes

Patients with significant hepatobiliary disease can have normal test results and conversely healthy patients can have abnormal test results. This lecture will focus on asymptomatic patients with elevated liver enzymes as it can be difficult to know how to proceed when a patient presents with abnormal liver enzymes but no clinical signs.

Markers of hepatocellular damage: alanine aminotransferase (ALT) and aspartate aminotransferase (AST)

ALT is found in high concentrations within the cytoplasm and mitochondria of hepatocytes. It is considered the best marker for hepatocellular injury in dogs and cats. ALT activity is relatively liver specific but can occasionally be increased due to muscle injury. Correlation with serum creatinine kinase activity is useful for differentiating ALT of muscle or hepatic origin. Serum levels depend on both the number of hepatocytes affected and the severity of injury but do not correlate with reversibility of injury or hepatic function. For instance, an acute severe injury can cause markedly high enzyme activity, but may be mostly reversible without signs of liver dysfunction. On the other hand, end-stage liver disease may only have slight increases in enzyme activity because of a marked decrease in the number of hepatocytes. Judging the magnitude of a change in serum enzyme values can be challenging. As a rule of thumb, a 2-3 fold increase above the reference interval is generally considered mild, where as a 4-5 fold increase is moderate, and as the value reaches closer to a 10 fold increase this is considered marked. Inflammatory or necrotizing disorders are generally associated with the largest increases (of the leakage enzymes). Serum or plasma ALT activity has been reported to have a half-life of about 40 to 61 hours in dogs and 3.5 hours in cats.

AST is also a marker of hepatocellular damage. This enzyme is present in significant quantities in skeletal muscle, brain, liver, kidney, erythrocytes, and cardiac tissue. Muscle damage and hemolysis can cause considerable increases in AST activity. AST is considered a less liver specific than ALT. The causes of an increased AST activity are similar to those of ALT. AST has a half-life of approximately 12 hours in dogs and 1.5 hours in cats

Markers of cholestasis: Alkaline phosphatase (ALP) and gamma-glutamyltransferase (GGT)

ALP is associated with the cell membrane in many tissues, including hepatocytes. Only liver and bone ALP in both cats and dogs and corticosteroid-induced ALP in the dog only, contribute significantly to serum activity. An elevated serum ALP activity can indicate primary hepatobiliary disease (ie cholestaisis), canalicular cell necrosis, or alternatively

increased hepatic synthesis. ALP is considered a sensitive marker for cholestasis. An elevated serum ALP activity does not distinguish between intrahepatic and extrahepatic cholestasis. A wide variety of diseases can cause intrahepatic cholestasis through hepatocyte swelling, leading to obstruction of small bile canaliculi and extrahepatic cholestasis. An increase in the serum ALP activity can be induced by endogenous, topical or systemic glucocorticoids, anticonvulsant medications, and possibly other drugs or herbs. ALP activity measurement has a high sensitivity (80%) for hepatobiliary disease, but its specificity is low (51%). The serum half-life of liver ALP is approximately 70 hours in the dog and 6 hours in the cat.

GGT is a membrane-bound enzyme found in biliary epithelial cells and hepatocytes. It is also found in pancreatic, renal tubular, and mammary gland epithelial cells. Elevations are usually caused by cholestasis or biliary hyperplasia resulting in enzyme induction. GGT may be a more sensitive indicator of hepatobiliary disease in cats than ALP, owing to the shorter half-life of ALP in cats. A notable exception is hepatic lipidosis, as moderate to marked increases of ALP are often seen with no to minimal increases in GGT. In dogs, it is thought to be less sensitive, but more specific, for liver damage than ALP. Corticosteroid administration and hyperadrenocortiscm can cause increased serum GGT activity in dogs, likely due to enzyme induction, but serum GGT is less influenced than ALP by enzyme-inducing drugs. Phenobarbitol can cause a transient increase in GGT. GGT has a half-life of approximately 72 hours in dogs

Tests of Liver Function:

1. Markers of hepatic synthetic function:
On the chemistry panel, it is important to assess the liver functional parameters which include bilirubin, albumin, glucose, BUN, and cholesterol. A reduction of approximately 70% to 80% of hepatic function must be present before a decrease in BUN, cholesterol, glucose and albumin are observed. Therefore these abnormalities are not considered sensitive indicators for the diagnosis of hepatobiliary disease. Also, changes in these analytes also occur due to many other non-hepatic diseases.

2. Bile Acids:
The most sensitive function test available are serum bile acids. Increases in fasting or postprandial serum bile acids concentrations are consistent with hepatic dysfunction, portosystemic shunting, or cholestasis. Bile acids should NOT be run in patients with an elevated bilirubin concentration. Bile acid concentrations >25-30 µmol/L in dogs and > 25 µmol/L in cats are suggestive of hepatobiliary disease, i.e. decreased functional mass, alterations in portal circulation. It is important to note that increases in bile acids have also been documented with tracheal collapse, gastrointestinal disease, and hyperadrenocortism. Most animals with congenital or acquired portosystemic shunting have markedly increased post-prandial bile acids concentrations, typically > 100 umol/L.

3. Ammonia:
Ammonia is not commonly performed in patients with suspected liver disease as it is not very stable in plasma samples, therefore an in-house analyzer is needed to reliably measure ammonia. Elevations in serum ammonia generally are associated with hepatic encephalopathy. Ammonia elevations best reflect portosystemic shunting rather than direct parenchymal damage as it has been suggested that a greater than 70% reduction of hepatic function is required for serum ammonia concentration to be increased.

Work-Up: General Guidelines

In an asymptomatic patient with increased liver enzymes, the value should be confirmed at least once. Once confirmed, the next step is a careful history to exclude drug/toxin associated enzymes elevations (see list below) or signs that may indicate an extrahepatic cause such as cushing's (dog), hyperthyroidism (cat), etc as a possibility. Additionally, a CBC, full chemistry panel, and urinalysis +/- total T4 should also be performed to look for other hints that may indicate the underlying cause of the hepatopathy such as microcytosis seen with some portovascular anomalies, glucosuria in some dogs with copper storage hepatopathy, etc.

If no likely cause for the elevation in liver enzymes can be found, such as drug induced or extrahepatic disease, there are two paths one could go down: 1) recheck liver enzymes in ~ 4 weeks or 2) begin a further diagnostic evaluation (abdominal ultrasound and/or bile acids testing). As a general rule if there is persistently elevated liver enzyme activity, I typically begin with an abdominal ultrasound followed by bile acids testing unless I am primarily concerned with a congenital portosystemic anomaly, in which case I lean toward a bile acids test as my initial diagnostic.

Imaging:
Routine abdominal radiographs are helpful in determining liver size and shape. An abdominal ultrasound is noninvasive, readily available and is the most informative initial imaging modality for liver disease. It is most valuable for assessing for hepatic masses, vascular anomalies, and diffuse change in the liver parenchyma. It is important to note that a sonographically normal liver does not rule out significant hepatic disease or even a hepatic mass. A study in 2013, found that 64% of sonographically unremarkable livers had histologic abnormalities. Ultrasound is also very useful for evaluation of the gallbladder and biliary tree. Gallbladder mucoceles, choleycystitis, choleliths, and intrahepatic or extrahepatic bile duct dilatation can be identified.

Sonographic abnormalities of the liver or of the gallbladder may warrant a fine need aspiration for cytological evaluation or percutaneous ultrasound-guided cholecystocentesis for cytological evaluation and culture. Primarily, I use cytological evaluation in an asymptomatic patient to assess for cancer in the liver and infection in the biliary tree. It is not useful for diagnosing inflammatory disease in the liver.

If the ultrasound is normal, then I assess the following factors to determine if more of a diagnostic evaluation is needed. 1) Signalment of the patient, 2) Enzyme pattern (cholestatic vs leakage vs mixed), 3) severity and duration of elevation, 4) abnormal functional testing.

1. Signalment: Signalment may be helpful since several breed-associated hepatopathies and portosystemic vascular anomalies have strong breed associations. If I find an elevated ALT in these patients, I am more inclined to recommend a further diagnostic workup rather than ongoing monitoring or trial with empirical therapy.

Copper-associated chronic hepatitis: Bedlington terriers, Labrador retriever, Dobermans, Skye terriers, West Highland white terriers, American/English Cocker Spaniels, English Springer Spaniels, Dalmatians, Siamese and European shorthairs

Idiopathic chronic hepatitis: Doberman pinchers, Cocker spaniels, Standard Poodles

Congenital portosystemic anomalies:
Intrahepatic Shunts: Maltese terriers, Yorkshire terriers, Havanese terriers, Pugs, Miniature schnauzers
Extrahepatic shunts: Irish wolfhound, Retrievers, Australian cattle dog, Austrailian Shepherd
Portal vein hypoplasia (formerly referred to as microvascular dysplasia): Miniature poodles, Yorkshire terriers, Maltese terriers (similar breeds to intrahepatic shunts)

Lobular Dissecting Hepatitis: Standarad poodles, American Cocker Spaniels

Gallbladder mucoceles: Shetland sheepdogs, cocker spaniels

2. Enzyme pattern, severity and duration of enzyme elevation(s), and functional testing results
Further diagnostic testing is also indicated if the patient in question is not of a breed predisposed to a hepatopathy, has no history of drug exposure, and has any of the following: 1) An elevation of greater than three times the upper reference range limit in ALT that is repeatable at least once, 2) progressive increase in enzyme activities, 3) single enzyme activity elevation with concurrent increase in bilirubin or decreased albumin concentration, 4) elevated bile acids. It is also warranted to further evaluate mild chronic elevations of any single enzyme.

General guidelines for increases in ALT activity or ALT>> ALP:
As stated above, the next diagnostic work up for an elevated ALT includes an abdominal ultrasound and bile acids testing. It is important to note that both of these tests can be normal despite liver disease being present. If abdominal ultrasound and bile acids are normal, the next step is either a liver biopsy or treatment trials with hepatoprotectants or antibiotics. In cats, I lean toward an antibiotic trial over hepatoprotectants with either

clavamox OR marbofloxacin and metronidazole for possible bacterial cholangitis. In dogs, I usually lean toward a hepatoprotectant trial unless the ultrasound showed gallbladder sludge or cholecystitis. ALT values should then be rechecked ~2 weeks later (while still on antibiotic if trial was antibiotics was elected). If there is improvement, ongoing therapy is recommended for a total of 4-6 additional weeks. If values remain persistently elevated a liver biopsy is recommended.

General guidelines for solitary ALP elevation or ALP >>ALT elevations:
A common finding is an elevated ALP in an asymptomatic dog (uncommon in cats). If there are clinical signs such as polyuria, polydipsia, polyphagia, consider testing for hyperadrenocortism and examining for exogenous sources of steroid administration. If completely asymptomatic, the most likely causes include early gallbladder mucocele, nodular hyperplasia, idiopathic vacuolar hepatopathy, and hepatic neoplasia. The next step in these patients with persistently elevated ALP elevation is an abdominal ultrasound. If abdominal ultrasound is unremarkable, most of the time I will benign neglect these patients but will periodically monitor for large jumps in the ALP values (ie: jump from 800 to 3500) which would prompt me to repeat an abdominal ultrasound. I suspect that many of these dogs have idiopathic vacuolar hepatopathy.

Liver Biopsy
A biopsy is required for a definitive determination of the nature and extent of hepatic damage and to appropriately direct the course of treatment. The commonly used liver biopsy techniques in dogs and cats are percutaneous needle biopsy, laparoscopic liver biopsy, and surgical liver biopsy. Each has advantages and disadvantages. Generally speaking, surgical or laproscopic liver biopsies are preferred to tru-cut liver biopsies.

COMMON CAUSES OF ELEVATED HEPATIC ENZYME ACTIVITIES IN ASYMPTOMATIC DOGS AND CATS:

There are other causes of elevated liver enzymes in both symptomatic and asymptomatic patients that are not described below. In addition, it is important to note that not all of the patients with the disease processes described below are asymptomatic.

Reactive hepatopathies:
Reactive hepatopathies occur secondary to a primary disease process elsewhere in the body, often involving the splanchnic circulation, that damage the liver. Commonly the ALT and ALP are mild (<3 x elevated) and functional testing is normal. In these cases, histopathologic changes include inflammatory changes limited to the portal areas and are not accompanied by fibrosis or hepatocyte necrosis/apoptosis. In this case the liver lesions do not represent the primary problem and one should search for an extra-hepatic cause. A common culprit is gastrointestinal disease. Therapies that could be attempted include, diet change to novel protein or hypoallergenic diet or probiotic therapy.

Drug induced injury:
Drug-induced liver injury: includes but not limited to, acetaminophen, tetracycline, doxycycline, methimazole, doxycycline, anesthetic agents, arsenical compounds, carprofen, diazepam/oxazepam, griseofulvin, itraconazole, ketoconazole, lomustine, phenobarbital, phenytoin, primidone, mebendazole, methimazole, oxibendazole-diethylcarbamazine, tetracycline, clindamycin, nitrofurantoin, trimethoprim- sulfadiazine, azathioprine.
Drug associated ALP induction: herbal medications, phenobarbital or glucocorticoids.

Vacuolar hepatopathy (VH):
Hepatic vacuolar change is a common histological diagnosis in dogs, but not cats. VH in dogs is most often associated with hyperadrenocorticism (HAC). Other causes include congenital glycogen storage disorders, breed-specific disorders, hepatic nodular hyperplasia, and a variety of stress-associated secondary diseases. There is a subset of dogs that do not have an underlying disease leading to VH and these dogs are referred to idiopathic vacuolar hepatopathy. Scottish Terriers are reported to have a breed-specific syndrome associated with VH and elevated ALP. Most dogs are middle-aged to older. There does not appear to be a breed or sex predisposition other than in the Scottish terrier. I personally do not treat dogs with idiopathic vacuolar hepatopathy. There is no evidence that hepatoprotectants such SAMe or silamyrin are beneficial for this syndrome.

Congenital portosytemic vascular anomalies:
These include microscopic (portal vein hypoplasia/microvascular dysplasia) and macroscopic (congenital extrahepatic, intrahepatic portosystemic shunts, arteriovenous malformation) defects in vascular development. Clinical signs are directly related to the degree of diversion of portal blood flow around the liver, so patients with vascular anomalies may be asymptomatic in cases of mild shunting.

Hepatic Nodular Hyperplasia (dogs, not cats):
This is a benign process causing an increase in liver enzymes and histological changes that include macroscopic or microscopic hepatic nodules containing vacuolated hepatocytes. Liver function remains unchanged. The etiology is unknown but appears to be an aging change in dogs; most of those affected are greater than 10 years of age. Laboratory findings include an ALP increase (mean ALP ~600 IU/L), but some may have mild increases in ALT and AST concentrations. Ultrasound may be normal or may demonstrate larger nodules (many can be only microscopic and not observed on ultrasound). Biopsy confirms the diagnosis. No specific therapy is needed.

Cholangitis:
Inflammatory bile duct diseases are among the most common types of hepatopathy in cats. While many of these cats present ill, there is a subset that are largely asymptomatic. Feline cholangitis may be accompanied by pancreatitis, inflammatory bowel disease and cholecystitis. The two forms of cholangitis commonly encountered are neutrophilic

(infectious) cholangitis and lymphocytic (immune mediated) cholangitis. Biopsy is required to confirm the diagnosis of inflammatory cholangitis.

Bacterial cholangitis and cholecystitis (dogs and cats):
Bacterial cholangitis/cholecystitis is usually caused by an ascending bacterial infection from the gut, however hematogenous spread can also occur. Common bacterial isolates include E. coli, Enterococcus spp., Streptococcus spp., Clostridium spp. Aerobic and anaerobic culture of the bile is recommended in a patients undergoing further evaluation of elevated liver enzymes. Bacterial cholangitis can be diagnosed via percutaneous ultrasound-guided cholecystocentesis. The bile should be submitted for cytology and aerobic and anaerobic cultures. Treatment usually requires at least 4-6 weeks of appropriate antibiotic therapy.

Chronic hepatitis:
Common causes are copper storage (dogs >>>> cats) and immune mediated hepatitis. Infectious etiologies are an uncommon cause of chronic hepatitis, however if histopathology showed pyogranulomatous hepatitis a work up for an infectious agent should be pursued.

Hepatic tumors:
These can be primary or metastaic. Primary hepatic neoplasms are less common than metastatic neoplasms. Hepatocellular adenomas are common in dogs and are generally restricted to a single liver lobe. These tumors are very slow growing and do not metastasize. Hepatocellular carcinomas (HCC) are the most common primary liver tumor in dogs and second most common primary liver tumor in cats. These are malignant tumors that can be carry a good prognosis when they are comprised of a single large tumor and surgically resectable. HCC that are nodular or diffuse, carry a poor prognosis. The liver can also be involved in other malignant processes including malignant histiocytosis, lymphoma, and systemic mastocytosis.

In cats, neoplasms of the biliary system (bile duct adenocarcinomas) occur more frequently than neoplasms of hepatic cell origin. Lymphoma and mast cell neoplasia occur relatively frequently as well.

In summary:
Abnormal liver enzymes in asymptomatic patient that are persistent and can't be attributed to an extrahepatic cause, should be further investigated. Ultimately, a liver biopsy is required for most patients to obtain a definitive diagnosis. If financial constraints limit a further workup, trials with hepatoprotectant therapy or antibiotic therapy can be trialed.

References:

Berent AC, Tobias KM. Portosystemic Vascular Anomalies. Vet Clin Small Anim. 2009; 513-541.

Lawerence YA, Steiner JM. Laboratory Evaluation of the Liver. Vet Clin Small Anim: 2017: (47) 539–553.

Libury, JA. Getting the Most Out of Liver Biopsy. Vet Clin Small Anim. 2017: 569–583

Muller PB, Taboada J, Hosgood G, et al. Effects of Long-Term Phenobarbital Treatment on the Liver in Dogs. J Vet Intern Med 2000;14:165–171.

Otte CM, Penning LC, Rothuizen J. Feline Biliary Tree and Gallbladder Disease Aetiology, Diagnosis and Treatment. Journal of Feline Medicine and Surgery. 2017: 514–528

Webster CRL, Center SA, Cullen JM, et al. ACVIM consensus statement on the diagnosis and treatment of chronic hepatitis in dogs. J Vet Intern Med. 2019; 33:1173–1200.

Feline Urethral Obstruction

Ladan Mohammad-Zadeh, DVM, DACVECC

DoveLewis Annual Conference Speaker Notes

Feline urethral obstruction is a common emergency condition. It has variable severity in its presentation, course of disease and prognosis. There are numerous underlying causes including urolithiasis, crystalline urethral plugs, and obstructive idiopathic disease. The nomenclature has changed in an effort to best describe the idiopathic form. We hesitate to use histologic terms like interstitial cystitis because there may be multiple etiologies for cystitis that result in the clinical syndrome that we are all familiar with. Feline Lower Urinary Tract Disease, Feline Urologic Syndrome, and Feline Idiopathic Cystitis are all terms people use to describe the constellations of signs we see in cats when urinary tract infection, uroliths or other defined causes have been ruled out. The pathogenesis of the idiopathic form is not well understood and involves many proposed risk factors including diet, environment, neutered status, body weight and even seasonality. We have come to recognize that indoor, male neutered, overweight cats on dry food are at higher risk for developing urethral obstruction. There has not been much new research in the last 10 years evaluating risk factors. But Jukes 2018 published a study aiming to better characterize the body condition aspect as a risk factor for urethral obstruction. It was a retrospective study examining 195 cats who presented for urethral obstruction compared to 195 control cats seen during the same time period. Their findings showed that while the incidence of urethral obstruction was not associated with increasing body weight, it was associated with increasing body condition score. The risk for developing urethral obstruction doubled for each body condition score above 4 (BCS out of 9).

Catheter size and duration of dwell time of catheter

Hetrick 2013 presented data that suggested there was an advantage in cats that had a 3.5 french urinary catheter placed. These cats had less recurrence of urethral obstruction at

24 hours (3.5 Fr 7/105, 6.67% v. 5 Fr 11/58, 18.97%; p = 0.017) and 30 days (3.5 Fr 14/82, 17.07% v. 5 Fr 16/51, 31.37%; p = 0.055) post catheter removal compared to a 5 Fr catheter. A reasonable explanation for this finding could be that the larger size of the catheter is more irritating thereby prolonging urethral inflammation.

The dwell time of the urinary catheter is somewhat arbitrary and varies greatly by clinician and by case. For the run-of-the-mill urethral obstruction with very little grit or blood in the urine that was easy to unblock, we usually keep the urinary catheter in for 24 hours, sometimes less. Through the literature the dwell time varies greatly as well, from as little as 12 hours to as long as 60 hours. Only one author specifically looked at catheter dwell time and impact on recurrence rates in a prospective manner. Eisenberg 2013 evaluated 68 cats from admit through follow up at 30 days post discharge. Ten out of the 68 cats reblocked within 30 days of discharge. The mean catheterization time for the cats that reblocked within 30 days was 21 hrs and 32 hrs for those that did not reblock within that time frame.

Management Post Discharge

Nivy 2019 evaluated 51 cats in a prospective randomized manner two treatment protocols post discharge. All cats were unblocked and treated per clinician preference. No cat received ketamine nor an alpha 2 agonist. All cats were given phenoxybenzamine during hospitalization. Nearly all the cats had a 5 Fr urinary catheter placed. Median duration of urinary catheter indwell time was 2 days. Median duration of hospitalization was 3 days. Cats were discharged with phenoxybenzamine 2mg/cat q 12 hr, and alprazolam 0.125 mg/cat q12h for 2 weeks. Twenty four were additionally given 0.025 mg/kg/day PO meloxicam and the remaining 27 cats were not. The addition of meloxicam did not influence recurrence rate. Overall recurrence rate of obstruction at 10 days was 1(2%), at 1 month 2 (4%), and 8 (16%) by 6 months.

Hetrick 2013 published a retrospective study involving 192 cats with urethral obstruction secondary to idiopathic disease. They examined the relationship between different management strategies and risk of recurrence of urethral obstruction. There was significantly higher recurrence rate of urethral obstruction in cats given phenoxybenzamine at both the 24 hours (phenoxybenzamine 10/46, 21.74% v. prazosin 10/140, 7.14% $p = 0.006$) and 30 days (phenoxybenzamine 16/41, 39% v. prazosin 20/110, 18.18% $p = 0.008$) after pulling the urinary catheter. Phenoxybenzamine is non-selective alpha 2 adrenergic antagonist which takes several days to reach maximum efficacy. Whereas prazosin has greater alpha-2 adrenergic affinity and a shorter onset of action which could explain improved outcomes post discharge.

Dorsch 2016 set out to evaluate the effect of meloxicam on the recurrence rate of cats with urethral obstruction. Thirty seven cats with urethral obstruction were treated with an indwelling urinary catheter and buprenorphine for 2 days. Cats were randomly assigned to additionally receive meloxicam or placebo after the first 24 hours of hospitalization for 5 consecutive days. Meloxicam was administered at 0.1 mg/kg for the first dose then 0.05 mg/kg q 24 hours for 4 days. Cats were only followed one week out from initial presentation. The recurrence rate of urethral obstruction within that 4 day period after discharge was similar between groups, 4/18 cats (22%) in the meloxicam group and 5/19 cats (26%) in the placebo group. At home evaluation of pain behavior, voiding behavior, food intake and general demeanor was reported to be similar between groups. It is commonly thought that robenacoxib is better tolerated than either meloxicam or carprofen and is FDA approved for post-surgical pain in cats for up to 3 days. One larger study in 2016 in 194 cats showed that daily robenacoxib dose ranging 1-2.4 mg/kg per day for 28 days was well tolerated even in cats with CKD.

Reineke 2018 attempted a prospective double blinded study in which 27 cats were administered 0.25 mg q 12hr prazosin and 20 cats were administered placebo for 30 days following urinary catheterization for urethral obstruction. There was no significant difference in the recurrence rate for obstruction post discharge between groups at 1 month

(prazosin 7%, placebo 5%) or 6 months (prazosin 15%, placebo 17%). Interestingly there was a difference noted in the median catheterization time (prazosin 32 hr v. placebo 39 hr, $p = 0.02$) and hospitalization time (prazosin 37 hr v. placebo 46 hr, $p = 0.036$) between groups. This could have been purely coincidence because there are numerous factors involved with deciding when to remove a urinary catheter from patient compliance to mechanical problems with the catheter to time of day. Also the difference in their results compared to a previous study could be the dose of prazosin used which was half the dose used in the Hetrick study. Nonetheless, the theoretical benefit of prazosin and the relatively low adverse effects makes it a reasonable choice to use as long as the administration of the medication at home does not add to stress on the cat.

Medical management, conservative management of UO

Sometimes hospitalizing a cat with an indwelling urinary catheter is outside of an owner's financial means. In these cases a veterinarian might do a "drive by unblocking" and hope for the best, giving the owners a strong warning that there is high likelihood their cat will reblock. Two papers examine this scenario using different treatments, one using medical management only without catheterization, and the other comparing one-time passing of urinary catheter to an indwelling urinary catheter.

Cooper in 2010 evaluated the use a medical management protocol without urethral catheterization in a group of cats. Fifteen male cats in which conventional treatment for urethral obstruction was declined by the owners were enrolled in the study. All cats were deemed to be metabolically stable and did not have radiopaque calculi. Cats were given acepromazine, buprenorphine, and medetomidine up to three times daily to keep cats comfortable and relaxed. Decompressive cystocentesis was performed up to 3 times per day and subcutaneous fluids were administered 1-2 times daily as needed. Success was determined if voluntary voiding was noted within 72 hours of implementing treatment. This medical management strategy was successful in 11 of 15 cats. The cats who failed therapy developed uroabdomen (3) or hemoabdomen (1). Cats in the treatment failure

group had significantly higher creatinine compared to cats in the successful group (10.10 mg/dL compared to 4.4 mg/dL, $p < 0.05$). On 3 week follow up call to the clients, 2 of the 11 remaining cats had an additional occurrence of urethral obstruction.

Seitz 2018 compared the outcome in 107 cats, half of whom were treated with a one-time unblocking and passage of a urinary catheter (outpatient group) and half who were treated with standard of care with an indwelling urinary catheter (in patient group). Cats with prior obstructions, urinary calculi, urethral tear among other reasons were not included in this study. There were no differences in biochemical abnormalities, physical exam findings or difficulty in unblocking between groups. Sedation and treatment with buprenorphine and prazosin (among other medications) were similar between groups. Recurrence rate of urethral obstruction within 30 days was higher in the outpatient group compared to the inpatient group (14/45, 31% vs. 5/46, 11%; $p = 0.018$). This roughly translates into a 3 times higher risk of recurrence of urethral obstruction after a one time urinary catheterization and treatment as an outpatient. Out of all of the cats that reblocked, 18/19 reobstructed within 1 week of removal of the urinary catheter.

Decompressive cystocentesis has some proposed benefits including providing patient relief, expediting resolution of metabolic disturbances prior to definitive unblocking and reducing intraluminal pressure facilitating placement of the urinary catheter. The biggest risk, of course, is bladder rupture and resultant uroperitoneum. Hall 2015 retrospectively examined the risk of bladder rupture in 47 cats that had decompressive cystocentesis prior to unblocking. They used a 22 ga 1.5 inch needle with an extension set to remove the urine. Mean dwell time for the catheter was 28 hours and hospitalization time was 40 hours. None of the cats were assessed as having developed uroperitoneum. Loss of detail cranial to the bladder was noted on over 50% of radiographs taken, however no fluid was obtained from the abdomen in any cat. It should be noted that loss of detail cranial to the bladder can be seen even without prior cystocentesis and likely represents local inflammation secondary to the obstructed urinary bladder. In cases where the clinician

identifies decreased detail cranial to the bladder, the presence of fluid should be confirmed via ultrasound and obtained for evaluation if possible.

Antibiotic use in UO

It is generally agreed that primary urinary tract infection is an uncommon cause for feline urethral obstruction. But there is some debate about antibiotic use in these cats because of the possibility of UTI associated with urinary catheter placement. Previous studies looking at this are over 10 years old and showed varying results and methodology was different between studies. Cooper 2017 reported findings from a prospective observational study in 31 cats with urethral obstruction. The study obtained urine cultures on presentation as well as q 24 hours until urinary catheter removal. No cat had a positive urine culture on presentation. Four of 31 cats (13%) had positive urine cultures from urine samples obtained 24 hours after urinary catheter placement. Streptococcus spp and Pasteurella spp were identified. The authors could not strongly recommend empirical antibiotic based on these findings.

Fluid therapy

Clinicians are lucky to have numerous fluid types at their disposal nowadays. It is most common to generally choose a buffered isotonic balanced crystalloid (LRS, Plasmalyte, Normosol R) for volume replacement. However there are a few specific indications for 0.9% NaCl which is not buffered and does not have any supplemental electrolytes other than sodium and chloride. Severely affected urethral obstruction patients can have life threatening hyperkalemia. Some clinicians might prefer 0.9% NaCl over another crystalloid because it is completely potassium free. A few studies in the recent past have shown that the reduction in potassium is not hindered by the use of potassium containing fluid and there is a slightly longer time to resolution of acid base status with the use of 0.9% NaCl, an inherently acidic fluid.

The fluid rate in cats with urethral obstruction is also debatable. There are reasonable guidelines for the initial phase if the cat is hypovolemic and in shock. However once the urinary catheter is placed and they are deemed more stable, fluid rates vary widely depending on institution and clinician preference. Two times "maintanence" fluid rate is a reasonable starting fluid rate which can adjusted based on the presence of post obstructive diuresis or patient risk factors such as heart disease. The important thing is to constantly monitor urine output and calculate ins and outs over several hours to determine if fluid rates need to be adjusted. Be aware that urine output is influenced by fluid administration. Thus making the determination as to when post obstructive diuresis has resolved can be tricky.

Perineal urethrostomy

Indications for a perineal urethrostomy include urethral tear past which a urinary catheter cannot be placed, and chronic recurrent urethral obstruction refractory to appropriate duration of medical management. Decades ago PU surgeries were thought of as a first line treatment for urethral obstruction but now are considered a salvage procedure when other treatments have failed. It is important to fully work up these cases prior to surgery to ensure no other significant co-morbidities will hinder recovery. Urine culture, abdominal ultrasound (or at least focal bladder ultrasound) and contrast urethrogram are ideal diagnostics prior to performing a PU surgery.

Savvy owners who do an internet search may express interest in having a PU surgery done for their cat with a first time urethral obstruction. It is very important that the client understand what a PU is not; A first line treatment for urethral obstruction, not even a second line treatment for urethral obstruction, a quick fix, or the answer to all the cat's problems. We must be mindful that not all anatomical locations along the urethra are amenable to PU and the surgery does nothing to address underlying cystitis if present. Perineal urethrostomy is a major surgery. The complication rate is variable but reported to be as high as 25%. Short term complications include UTI and hemorrhage, and long term

complications include urinary and fecal incontinence and urethral stricture. Surgeon experience does play a role in the complication rate thus referral to a center with surgeons experienced with this procedure may help ensure a better outcome.

Feline urethral obstruction is a great example of treatment evolving through good research. How we approach this condition is very different than 20 years ago. Unlike other disease conditions there's no single accepted approach to management. There are "reasonable recommendations" based on the literature; 3.5 Fr urinary catheter instead of 5 Fr, leaving urinary catheter in for at least 24 hours, using Prazosin over phenoxybenzamine, starting antibiotics only if culture positive (or maybe not?). Client education continues to be important regarding at home management and recurrence rates. Perineal urethrostomy should be a last resort treatment option for the management of this condition.

Citations

Beer KS. Severe anemia in cats with urethral obstruction: 17 cases (2002–2011). JVECC. 2016; (26)3.

Brabson TL. Correlation of gross urine color with diagnostic findings in male cats with naturally occurring urethral obstruction. J Feline Med Surg. 2015;17(6):453-457.
Cooper ES. A protocol for managing urethral obstruction in male cats without urethral catheterization. JAVMA. 2010; 237:1261–1266

Cooper ES. Incidence of bacteriuria at presentation and resulting from urinary catheterization in feline urethral obstruction. JVECC. 2019;29(5):472-477.

Cooper ES. Controversies in the management of feline urethral obstruction. JVECC. 2015; 25(1): 130-137.

Dorsch R. Evaluation of meloxicam for the treatment of obstructive feline idiopathic cystitis. J Feline Med Surg 2016;18(11): 925-933.

Eisenberg BW. Evaluation of risk factors associated with recurrent urethral obstruction in cats treated medically for urethral obstruction. J Am Vet Med Assoc 2013; 243:1140–1146.

Hall J. Outcome of male cats managed for urethral obstruction with decompressive cystocentesis and urinary catheterization: 47 cats (2009–2012). JVECC. 2015;25(2).

Hetrick FP. Initial treatment factors associated with feline urethral obstruction recurrence rate: 192 cases (2004-2010). JAVMA. 2013;243(4):512-519.

Jukes A. Associations between increased body condition score, body weight, age and breed with urethral obstruction in male castrated cats. Vet J. 2019;244:7-12.

Nivy R. A Prospective randomized study of efficacy of 2 treatment protocols in preventing recurrence of clinical signs in 51 male cats with obstructive idiopathic cystitis. JVIM. 2019;33(5):2117-2123.

Nye AK. Feline perineal urethrostomy: a review of past and present literature. Top Companion Anim Med. 2018; 33(3):77-82.

O'Hearn AK. Coccygeal epidural with local anesthetic for catheterization and pain management in the treatment of feline urethral obstruction. JVECC. 2011;(21)1

Reineke EL. The effect of prazosin on outcome in feline urethral obstruction. JVECC. 2017;(27) 4.

Seitz MA. Evaluation for association between indwelling urethral catheter placement and risk of recurrent urethral obstruction in cats. JAVMA. 2018;252 (12): 1509-1520.

Slater MR. Welfare of cats 5-29 months after perinueal urethrostomy: 74 cases 2015-2017. J Fel Med Surg. August 2019.

Watson MT. Evaluation of postoperative complication rates in cats undergoing perineal urethrostomy performed in dorsal recumbency. J Feline Med Surg. March 2019.

Preventative Medicine:

Avoiding burnout and compassion fatigue together

Shana O'Marra, DVM, DACVECC

DoveLewis Annual Conference Speaker Notes

Burnout and compassion fatigue are well-recognized problems in healthcare professions. Apart from the personal physical and mental health toll on the individual, compassion fatigue and burnout can contribute to poor job performance and employee turnover. The world of veterinary medicine shares many risk factors for burnout with human healthcare fields, but has the potential for even greater risk given the direct financial pressures on the care we deliver.

The concepts of compassion fatigue and burnout are often conflated. This is not surprising given that symptoms of emotional, mental and physical exhaustion and a feeling of isolation and loss of meaning are common to both syndromes. The major difference between the two is the underlying cause or trigger. Compassion fatigue arises from the secondary trauma of caring for others and can follow an individual wherever that relationship might exist. Burnout arises from the relationship an individual has with a workplace and is specific to the environment. Compassion fatigue can come on very suddenly from a particularly traumatic experience, but burnout always has a gradual onset as a consequence of building stressors. Not surprisingly, although cultivating self-awareness and coping skills can help with both situations, interventions on the organizational level have been shown to be more effective in preventing and treating burnout.

Although burnout is often characterized in popular culture as simple exhaustion due to an overload of work, research has demonstrated that a more complex model of burnout is a better predictor of which individuals will suffer from burnout as well as what interventions

are most likely to be effective. Maslach and Leitner's three dimensional definition of burnout acknowledges that burnout encompasses the experience of exhaustion, cynicism or depersonalization, and feelings of professional inefficacy.

There are multiple models to describe how professional burnout develops. The Jobs-Demands-Resources model proposes that burnout occurs when work demands chronically outstrip the resources and the individual does not have power to alter demand. Similarly, the Conservation of Resources model suggests that burnout develops when an individual perceives persistent threat to available resources. These two models, while straightforward and easy to understand, neglect the moral and ethical realm as contributors to burnout. The Areas of Worklife model postulates that burnout arises when there is a mismatch between the individual and the workplace across six domains:

- Workload
- Control
- Rewards
- Community
- Fairness
- Values

This model was developed directly from research identifying risk factors for burnout. Interestingly, while workload mismatch, or work overload was a good predictor of the exhaustion component of burnout, it was a much less powerful predictor of the burnout in general. It is important to note that the domain of reward refers not just to compensation or recognition, but also to the concept of joy in work. The values domain holds particular importance in veterinary medicine, where moral distress is common, with one recent study documenting that 62% of survey veterinarians felt they were not able to "do the right thing" sometimes or often in their professional life. Even though they represent very different aspects of work, the six domains are necessarily interconnected, and in individuals suffering from burnout, improving one domain often lifts the others. Even small interventions can have large effects, suggesting that even partial measures are worth the time and effort.

Because of the financial burden on human healthcare, resources are now being directed to useful research and evidence-based models for preventing burnout in human healthcare systems. A recent meta-analysis found that physicians having more control over their jobs, fostering a sense of teamwork and increasing the level of communication among team members were the most effective interventions (Panagioti et al). The Mayo Clinic (https://doi.org/10.1016/j.mayocp.2016.10.004), the Institute for Healthcare Improvement (IHI.org) and other initiatives have developed frameworks for institutional change to address and prevent burnout. Many of these strategies can be translated on a smaller scale to veterinary medicine.

The growing awareness of mental health issues in the veterinary world has led to many positive changes. Much of the stigma for discussing these issues has dissipated, and self-care has been embraced as a necessary part of professional development. However, efforts to change the work environment rather than the individual have been largely lacking in veterinary medicine. Recognizing the nature of Burnout Syndrome means acknowledging the responsibility of the institution to prevent and mitigate burnout.

References:

Bakker AB, LeBlanc PM, Schaufeli WB. Burnout contagion among intensive care nurses. J Advanc Nurs 2005; 51: 276- 87.

Kearney MK, Weininger RB, Vachon ML, Harrison RL, Mount BM. Self-care of physicians caring for patients at the end of life: "Being connected… a key to my survival". JAMA. 2009 Mar 18;301(11):1155-64, E1

Leiter MP, Maslach C. Nurse turnover: the mediating role of burnout. J Nurs Manage 2009; 17: 331- 9.

Maslach, C. and Leiter, M. P. (2016), Understanding the burnout experience: recent research and its implications for psychiatry. World Psychiatry, 15: 103-111.

Maslach C, Leiter MP. The truth about burnout. San Francisco: Jossey-Bass, 1997.

Moore IC, Coe JB, Adams CL, Conlon PD, and Sargeant JM. Exploring the Impact of Toxic Attitudes and a Toxic Environment on the Veterinary Healthcare Team. Front Vet Sci. 2015; 2: 78.

Moses L, Malowney MJ, Wesley Boyd J. Ethical conflict and moral distress in veterinary practice: A survey of North American veterinarians. J Vet Intern Med. 2018 Nov;32(6):2115-2122.

Panagioti M, Panagopoulou E, Bower P, et al. Controlled Interventions to Reduce Burnout in Physicians: A Systematic Review and Meta-analysis . JAMA Intern Med. 2017;177(2):195-205

Patel R S, Sekhri S, Bhimanadham N N, et al. (June 03, 2019) A Review on Strategies to Manage Physician Burnout. Cureus 11(6): e4805.

Schaufeli WB, Leiter MP, Maslach C et al. Maslach Burnout Inventory – General Survey. In: C Maslach, SE Jackson, MP Leiter (eds). Maslach Burnout Inventory manual, 3rd ed. Palo Alto: Consulting Psychologists Press, 1996: 19- 26.

Schwartz SP, Adair KC, Bae J, et al. Work-life balance behaviours cluster in work settings and relate to burnout and safety culture: a crosssectional survey analysis. BMJ Qual Saf 2019;28:142–150.