Cytologic Evaluation of the Liver: Aspiration Findings and Limitations

University of Florida
Shashi K. Ramaiah, DVM, PhD
A. Rick Alleman, DVM, PhD, DACVP, DABVP

ABSTRACT: Cytologic examination of exfoliative specimens obtained during blind or ultrasound-guided aspiration of the liver is a useful procedure for diagnosing many liver diseases in dogs and cats. Although history; clinical signs; and biochemical, radiographic, and ultrasonographic evaluation are useful in localizing a disease process in the liver, microscopic evaluation is usually required to obtain a causative diagnosis and establish a prognosis and treatment plan. Tissue aspiration cytology is a valuable tool for determining the etiology of selected liver diseases because of the minimal risk in obtaining a sample and the relative quickness involved in sample preparation and interpretation. This article provides an overview of how cytologic smears obtained from the liver can be used to gain maximal information. Certain limitations of aspiration cytology are also discussed.

The liver is involved in nearly every biochemical process required to maintain normal body functions. Because of this, liver disease can result in systemic illness with clinical signs that are unpredictable and nonspecific, regardless of the inciting cause or etiology. The identification of liver disease is typically based on a combination of any of the following:

- **Clinical signs** (e.g., periodic ascites, intolerance of a high-protein diet, icterus, chronic weight loss, abnormally colored feces or urine, bleeding disorders)
- **Elevated liver enzyme activities** (e.g., alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase)
- **Hepatic function tests** (e.g., measurement of urea, albumin, bile acids, ammonia)
- **Radiographic abnormalities** (e.g., increased or decreased liver size, liver abscesses, abnormal mineralization, circulatory abnormalities)
- **Ultrasonographic evaluation of the liver** (e.g., size and density, visualization of the circulation and bile duct system)

Although these methods are required to localize a disease process in the liver, they rarely supply definitive information regarding the etiology of hepatic dis-
Pathologic evaluation is usually needed to obtain a causative diagnosis and establish a prognosis and treatment plan.

Histologic evaluation of the liver is the most definitive method of diagnosing liver disease. However, the invasive nature of obtaining a sample, the danger of hemorrhage due to coagulopathies associated with liver disease, and the time required for sample submission and preparation limit its use in clinical practice. Tissue aspiration cytology is a practical alternative for determining the etiology of selected liver diseases. This article reviews the basic techniques of sample collection and slide preparation of tissue aspirates collected from the liver. Significant cytologic findings are discussed and incorporated with clinical and laboratory findings to make a specific diagnosis. Limitations of the use of exfoliative cytology in the diagnosis of liver disease are also emphasized.

**INDICATIONS FOR CYTOLOGIC EVALUATION**

Clinical signs, increases in hepatic enzymes, alterations in hepatic function tests, and radiographic and ultrasonographic abnormalities are all indications for fine-needle aspiration of the liver. Conditions resulting in a generalized hepatomegaly usually yield cytologic preparations with the most diagnostic significance when aspirates are collected blindly. This signifies diffuse hepatic disease and offers the best opportunity for obtaining a representative sample without visual guidance. In addition, ultrasound-guided fine-needle aspirates are often very rewarding for cytologic evaluation of hepatic nodules and focal inflammatory disease and are considered an accurate, safe, and inexpensive means of characterizing focal hepatic lesions.

**SAMPLING TECHNIQUES**

**Fine-Needle Aspiration**

Although tissue aspiration, when properly performed, causes minimal damage and hemorrhage, it may be advisable in some patients to conduct a platelet count, activated clotting time, and buccal mucosal bleeding time to screen for bleeding abnormalities. A 22-gauge needle with a 12-ml syringe is best suited for aspiration of the liver. The use of an extension tube between the needle and syringe may provide better control during the aspiration procedure. Blind sticks can be performed with the animal in dorsal recumbency by tilting the body slightly to the right and inserting the needle to the left of the xiphoid cartilage, toward the diaphragm. The left lobe of the liver is the largest, and in this position, the gallbladder is usually located to the right of the midline. Aspirates may also be obtained from the left side just caudal to the last rib with the animal in ventral or right lateral recumbency. If the left lobe cannot be palpated beyond the edge of the last rib, radiographic evaluation may indicate the appropriate intercostal space for sample collection.

Once the sample is collected, the material should be quickly expelled from the hub of the needle onto a new, dust-free glass slide (Figure 1A). A second slide should be
gently placed on top of the first in order to spread the material in a monolayer of cells (Figure 1B). The two slides should then be gently slid apart and the material air-dried. Romanovsky-type stains, such as Wright-Giemsa or modified Wright-Giemsa (e.g., Diff-Quik [VWR Scientific], Leukostat [MD Depot Medical Supplies], Quik-Dip [Fisher Scientific]) are used for routine evaluation of liver aspirates. In addition to the previously mentioned routine stains, special stains can be used to identify specific materials seen on cytologic preparations and are available at any pathology reference laboratory (Table 1).

Once the sample is prepared, the cytologist’s first objective is to interpret hepatocellular changes and categorize these changes into one of the seven major cytopathologic categories (see box on p. 802).

**Normal Liver**

The ability to interpret hepatic cytopathology depends on the ability to recognize normal hepatocytes and biliary epithelium.

**Hepatocytes** are the predominant nucleated cell type in most liver aspirates. These large, fairly uniform cells usually occur in variably sized clumps and sheets. Hepatocytes can be round to polygonal with distinct cytoplasmic borders and abundant, lightly basophilic cytoplasm (Figure 2). The cytoplasm may appear lightly granular and occasionally contain one or two small, clear vacuoles. The nuclei are usually centrally located. Chromatin is stippled in appearance, and nuclei often contain a distinctive, large, single nucleolus. Binucleated hepatocytes may occasionally be seen in normal livers.

**Biliary epithelia** are infrequently observed in samples collected from normal livers. These cells, which are much smaller than hepatocytes, are very uniform and typically seen in small clumps. The cytoplasm is scant, and the nuclear:cytoplasmic ratio is high (Figure 3). Nuclei are slightly smaller than those of hepatocytes and are usually absent or indistinct. Low numbers of macrophages and mast cells may occasionally be seen in normal canine livers. Blood and blood elements are typically present, resulting from capillary damage during the aspiration process.

**Nodular Hepatic Hyperplasia/Hepatic Adenoma**

Nodular hepatic hyperplasia is a focal proliferation of hepatocytes and is a common finding in older dogs. It is cytologically indistinguishable from a hepatic adenoma (hepatoma). Hepatocytes often contain diffuse vacuolar change consistent with glycogen accumulation. There is a mild increase in nuclear:cytoplasmic ratio,

<table>
<thead>
<tr>
<th><strong>Stain</strong></th>
<th><strong>Material Detected</strong></th>
<th><strong>Reference Laboratory</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td>Prussian blue</td>
<td>Iron</td>
<td>Sigma-Aldrich, Catalog No. 234125</td>
</tr>
<tr>
<td>Congo red</td>
<td>Amyloid</td>
<td>Sigma-Aldrich, Catalog No. 60910</td>
</tr>
<tr>
<td>Fouchets reagent(Hall stain)</td>
<td>Bile</td>
<td>NewComer Supply, Catalog No. 1095B</td>
</tr>
<tr>
<td>Rubeanic acid</td>
<td>Copper</td>
<td>Harleco, Catalog No. 145160</td>
</tr>
<tr>
<td>Periodic acid–Schiff</td>
<td>Glycogen</td>
<td>SurgiPath, Catalog No. 03812</td>
</tr>
<tr>
<td>Oil red O</td>
<td>Fat</td>
<td>ProSciTech, Catalog No. C150</td>
</tr>
</tbody>
</table>

Table 1. Additional Stains for Evaluation of Specific Materials
of diffuse vacuolar change can be seen in a number of disease processes that can affect the liver (see p. 804). However, recognizing these changes in a nodular lesion, along with the additional findings mentioned, allows identification of this lesion as a hyperplastic nodule. Some hyperplastic nodules contain sites of extramedullary hematopoesis. In those cases, nucleated erythrocytes, megakaryocytes, and, rarely, immature leukocytes may also be identified cytologically.

**Hepatocellular Regeneration**

Hepatocellular regeneration is a nonspecific response...
to any number of disease processes that cause hepato-
cellular damage. A regenerative response is character-
ized by the presence of a mixture of normal to reactive-
appearing hepatocytes, along with scattered populations
of more immature hepatocytes (Figure 5). Reactive and
immature hepatocytes may often contain a more deeply
basophilic cytoplasm with higher nuclear:cytoplasmic
ratio than normal. Nuclei are variable in size and shape
(e.g., anisokaryosis, pleomorphism) and may have
prominent, multiple nucleoli. Intranuclear rectangular
inclusions are occasionally noted (Figure 6). Evidence
of necrosis and/or inflammation may also be observed
in the preparation.

Regenerative epithelium may exhibit nuclear features
that mimic malignancy. Therefore, these cytologic find-
ings must be interpreted with caution when there is
also evidence of normal hepatocytes, inflammation,
and/or necrosis in the preparation. The diagnosis of
hepatocellular carcinoma should not be made based
solely on the identification of anaplastic nuclear fea-
tures in a population of hepatocytes. This is a limita-
tion of cytopathology of liver aspirates. Nuclear abnor-
malities in the absence of a hepatic mass more often
represent a regenerative response to liver injury. How-
ever, when anaplastic features are of questionable ori-
gin, histopathology is suggested to confirm a diagnosis.

**Hepatocellular Necrosis and Vacuolar Changes**

Hepatocellular changes may be recognized in several
different conditions. The type of cellular changes pres-
ent can sometimes give an indication of the disease
process that caused hepatocellular damage. The two
types of cellular changes discussed are necrosis and vac-
ular change. Vacuolar change is further characterized
as either glycogen or lipid accumulation. Hydropic
change is difficult to identify cytologically and will not
be discussed.

As in other tissues, **necrosis** is characterized by the
presence of clumps of amorphous, basophilic material,
which are usually in the shape of cellular cytoplasm
(Figure 7). However, nuclei are absent or barely visible
in this cellular debris. Necrosis is a nonspecific find-
ing that may occur in numerous disease processes that
result in inflammation, vascular compromise, or toxic
damage.

**Vacuolar change** is a nonspecific term used to describe
changes in hepatocytes that result in intracellular deposit-
ing of glycogen, lipid, or water (hydropic change).
Glycogen accumulation appears cytologically as a diffuse cytoplasmic clearing or foamy vacuolation that is most prominent in the periphery of the cytoplasm. This may result in a characteristic perinuclear, cytoplasmic basophilia (Figure 8). In severe cases, the cytoplasmic distention may result in marked megalocytosis.

Glycogen accumulation (referred to as glycogen vacuolar change) can be seen in the hepatocytes of dogs with steroid hepatopathy, nodular hyperplasia, or idiopathic vacuolar degeneration. The hepatic cytopathology is the same for each of these disease conditions. The defining cause is identified by combining the cytologic findings with other chemical and laboratory findings. Glycogen accumulation most commonly occurs in the liver of animals with steroid-induced hepatopathies from Cushing’s disease or exogenous administration of glucocorticoids. Patients typically present with diffuse hepatomegaly and moderate to marked increase in serum–alkaline–phosphatase activities, with only mild to moderate increases in alanine aminotransferase activity and normal total bilirubin concentration. Other clinical signs associated with Cushing’s disease may also be observed. In these cases, the finding of hepatocellular glycogen accumulation is strongly supportive of a diagnosis of steroid hepatopathy. Glycogen accumulation can also be seen in aspirates obtained from patients with hepatic nodules (see p. 800) or idiopathic vacuolar hepatopathy. Therefore, if an ultrasound-guided needle aspirate was collected from a hepatic nodule, the cytologic finding of glycogen accumulation would have a different interpretation; the glycogen accumulation would be indicative of a hyperplastic hepatic nodule.

Idiopathic vacuolar hepatopathy is a poorly defined condition in dogs that is characterized by increased serum–alkaline–phosphatase activities and hepatocellular changes (glycogen) similar to those seen in animals with steroid-induced hepatopathy but no history of exposure to glucocorticoids. Patients typically present with diffuse hepatomegaly and moderate to marked increase in serum–alkaline–phosphatase activities, with only mild to moderate increases in alanine aminotransferase activity and normal total bilirubin concentration. Other clinical signs associated with Cushing’s disease may also be observed. In these cases, the finding of hepatocellular glycogen accumulation is strongly supportive of a diagnosis of steroid hepatopathy. Glycogen accumulation can also be seen in aspirates obtained from patients with hepatic nodules (see p. 800) or idiopathic vacuolar hepatopathy. Therefore, if an ultrasound-guided needle aspirate was collected from a hepatic nodule, the cytologic finding of glycogen accumulation would have a different interpretation; the glycogen accumulation would be indicative of a hyperplastic hepatic nodule.

In contrast to glycogen accumulation, hepatocytes with lipid accumulation contain discrete, punctate, clear cytoplasmic vacuoles (Figure 9). The vacuoles are sometimes so large and abundant that they distort normal cell morphology, making hepatocytes difficult to recognize. Severe lipid accumulation (also referred to as lipid vacuolar change) is almost exclusively seen in cats with hepatic lipidosis syndrome. However, mild to moderate lipid accumulation can be seen as a secondary response to hepatocellular damage resulting from numerous disease conditions, such as diabetes mellitus, pancreatitis, cholangiohepatitis, or hepatic lymphoma. Animals with steroid-induced hepatopathy may also have some lipid accumulation along with glycogen in the hepatocytes. The presence of lipid accumulation can be confirmed and distinguished from hydropic change by using Oil Red O stain (Table 1).

Cholestatic Disease

Cytologic evidence of hepatic cholestasis is characterized by the presence of dark blue to black bile pigment seen within the cytoplasm of hepatocytes or in casts coursing between adjacent hepatocytes in a clump (Figure 10). This is a common finding in many hepatobiliary disorders and precedes the onset of icterus. Accumulation of bile pigment is seen in any animal with extrahepatic or intrahepatic biliary stasis. It also occurs frequently in some of the degenerative conditions (e.g., hepatic lipidosis, steroid-induced hepatopathies) mentioned.

In cytologic preparations of the liver, the presence of dark pigment is most frequently bile. However, with Diff-Quik and other Romanovsky-type stains, bile pigment cannot be distinguished from accumulation of hemosiderin (which can be seen in the liver of patients with hemochromatosis, hemolytic anemia, or chronic inflammatory disease) and sometimes copper. The stains listed in Table 1 may aid in cases in which cytochemical identification of pigment is necessary.
Inflammatory Disease

Because of the large amount of blood contamination associated with liver aspirates and the focal nature of many inflammatory lesions, the cytologic identification of inflammatory liver disease may be difficult. The negative finding for inflammation on cytology does not rule out an inflammatory disease process. The inability to consistently identify the presence of inflammatory disease is a major limitation of hepatic cytopathology. However, once this limitation is recognized, the practicing cytologist is aware that the presence of inflammatory disease cannot be ruled out on the basis of cytology alone. Nevertheless, when present, inflammation is a significant finding on cytologic preparation of liver aspirates. Inflammatory processes in the liver are similar to those in other tissues; they can be classified as neutrophilic, lymphocytic, mixed, and eosinophilic inflammation.

**Neutrophilic inflammation** is characterized by the presence of neutrophils above the number that would be expected if blood contamination has occurred. Neutrophils are particularly significant if they are associated with clumps of hepatocytes or if there is accompanying evidence of hepatic necrosis or degeneration (Figure 11). Neutrophilic inflammation is usually associated with bacterial sepsis and may be seen with suppurative hepatitis or feline suppurative cholangiohepatitis. The inflammatory process in suppurative cholangiohepatitis is usually periductular in location and may be inadvertently missed during aspiration. A chronic form of this disease also exists and is characterized by a mixture of inflammatory cells, including neutrophils and lymphocytes.

**Lymphocytic inflammation** is characterized by the presence of increased numbers of small lymphocytes and occasional plasma cells (Figure 12). This may be seen in cats with nonsuppurative periportal hepatitis, which is more common than suppurative hepatitis. The nonsuppurative form is believed to be a progression of the suppurative form. An immune-mediated component has been suggested for this form. Biliary cirrhosis may result from the chronic form. It is also important to note that aspirates from some cats with hepatic lymphoma may contain a large population of small, well-differentiated lymphocytes (see p. 808). These patients usually have severe hepatomegaly, whereas cats with nonsuppurative cholangiohepatitis (mild hepatomegaly) do not. Therefore, a population of small, well-differentiated lymphocytes in the liver of cats could be the result of either disease. The clinical presentation should provide information as to the likelihood of one disease process or the other. Histologic confirmation is recommended in feline patients with lymphocytic infiltrates, regardless of the cytologic appearance of the lymphocytes.

**Mixed inflammation** is characterized by the presence of macrophages and/or neutrophils and lymphocytes. A classic example of this type of inflammation occurs in dogs with chronic active hepatitis. As with other tissues, mixed inflammation may also be associated with some bacterial infections, such as mycobacterial, protozoal infections (e.g., cytauxzoonosis, toxoplasmosis), or systemic fungal infections (e.g., histoplasmosis).

The presence of an **eosinophilic inflammatory response** is uncommon in the liver. It may be seen in cats with liver flukes, hypereosinophilic syndrome, eosinophilic leukemia, or mast cell tumors. Additional laboratory and clinical findings may be needed to make a more definitive diagnosis.
Neoplasia

The diagnosis of hepatocellular carcinoma (HCC) is most reliable when anaplastic-appearing cells with some differentiation toward mature hepatocytes are aspirated from a hepatic mass. These cells have cytoplasm similar to that of hepatocytes, with nuclear features of malignancy, particularly high and variable nuclear:cytoplasmic ratio, anisokaryosis, and extremely prominent nucleoli, which are often large and singular but also multiple (Figure 13). Most HCCs in cats have significant cytologic criteria for malignancy and are aggressive neoplasms with metastasis in about 28% of cases. HCCs usually maintain some degree of hepatocyte differentiation and often can be easily distinguished cytologically from metastatic carcinomas. In dogs, the biologic behavior of HCC depends on the gross morphologic appearance of the lesion. As a result, the cytologic diagnosis of HCC should always be interpreted in the context of gross appearance.

Canine and feline HCCs occur in three distinct morphologic forms: diffuse, nodular, and massive. Grossly, the diffuse form consists of large areas of the liver infiltrated by nonencapsulated neoplastic tissue; the nodular form consists of multiple discrete nodules of variable size within several lobes; and the massive form consists of a solitary large mass affecting a single liver lobe. Diffuse and nodular forms in dogs (reported to be about 100% and 90%, respectively) are associated with high metastatic potential. The massive forms have a lower metastatic potential (reported to be about 35%). Some massive forms of HCCs in dogs appear as a fairly uniform population of cells with minimal criteria for malignancy. These often require histologic evaluation to be classified as well-differentiated carcinomas. It is cytologically impossible to distinguish a well-differentiated carcinoma from a large hepatic adenoma. However, the metastatic potential for the massive form of well-differentiated carcinomas appears to be low. Carcinomas may be found in any lobe of the canine liver, although they most commonly occur in the left lateral lobe. The presence of inflammation or clumps of normal-appearing hepatocytes and necrosis in combination with atypical-appearing hepatocytes warrants histopathologic confirmation because regenerative responses in hepatic tissue may mimic malignancy.

Bile duct carcinomas are malignant tumors of the bile duct epithelium. Cells aspirated from these lesions are smaller than hepatocytes and occur in dense clusters. Most cells have a very high nuclear:cytoplasmic ratio and contain scant, basophilic cytoplasm. Nuclear features of malignancy are usually present with the exception of nucleoli, which are smaller and more indistinct than those seen in HCC. It is difficult, if not impossible, to distinguish some bile duct carcinomas from metastatic carcinoma that may be seeded in the liver from other distant locations. Malignancies of splenic, pancreatic, adrenal gland, or intestinal origin can metastasize to the liver; information regarding these other tumors is discussed elsewhere.

Hepatic lymphoma is characterized by infiltration of abnormal lymphocytes into the liver parenchyma. In most dogs and some cats, these lymphocytes are large and immature (Figure 14). They are individually

---

**Figure 13**—HCC cells have a cytoplasm similar to hepatocytes; however, nuclear features of malignancy, such as high and variable nuclear:cytoplasmic ratio, coarsely clumped chromatin pattern, anisokaryosis, and multiple, extremely prominent nucleoli, are also observed. (Wright-Giemsa, original magnification ×250)

**Figure 14**—Hepatic lymphoma in dogs shows a neoplastic population of individually arranged, large, round lymphoblasts with scant amounts of deeply basophilic cytoplasm. Nuclei are round to polygonal and are at least twice the size of erythrocytes. The chromatin pattern is diffuse, and nucleoli can be seen. (Wright-Giemsa, original magnification ×125)
arranged round cells with scant amounts of deeply basophilic cytoplasm. Nuclei are round to polygonal and usually at least twice the size of erythrocytes. The chromatin is typically diffuse, and nucleoli are often seen. However, in some cats with hepatic lymphoma, the neoplastic cell population is composed of small, well-differentiated lymphocytes (Figure 15). This makes a definitive diagnosis of lymphoma more difficult because the lymphocytes in cats are cytologically indistinguishable from the inflammatory lymphocyte infiltrate that is seen with nonsuppurative cholangiohepatitis. Typically, liver aspirates obtained from cats with well-differentiated lymphoma have very high numbers of lymphocytes present. Cats with nonsuppurative cholangiohepatitis—because of the focal, periporal location of the infiltrate—have low to moderate numbers of lymphocytes present, if they are identified at all. In addition, the clinical presentation is useful in distinguishing between two disease processes. Cats with nonsuppurative cholangiohepatitis tend to be young adult males, often less than 4 years of age; hepatomegaly is mild, if present at all. With the exception of feline leukemia virus–positive cats, feline hepatic lymphomas usually occur in older cats. Unlike cats with nonsuppurative cholangiohepatitis, cats with hepatic lymphoma usually present with severe hepatomegaly.

Mast cells are rarely observed in aspirates of normal liver. However, metastatic mast cell tumors are characterized by the presence of large numbers of individually arranged round cells with abundant metachromatic, cytoplasmic granules (Figure 16). They are seen in the liver of more than 70% of dogs with systemic mastocytosis.

Aspirates taken from patients with hepatic hemangiosarcoma contain low numbers of anaplastic-appearing mesenchymal cells as well as large amounts of blood. The cells have a veil-like, pale blue cytoplasm that often contains small, clear cytoplasmic vacuoles (Figure 17). Hemangiosarcoma may be a primary hepatic neoplasm or may result from metastasis from the spleen or other distant location. One of the major limitations is the poor exfoliative nature of these tumors. As a result, cytopathologic diagnosis is sometimes not possible.

By definition, leukemia is a malignancy of hema-

Figure 15—Some feline hepatic lymphomas contain a neoplastic population of individually arranged small, well-differentiated lymphocytes. Nuclei are only 1 to 1.5 times the size of erythrocytes, and the nuclear chromatin pattern is dark and dense. (Wright-Giemsa, original magnification $\times 125$)

Figure 16—Hepatic mast cell tumors contain large numbers of individually arranged round cells with abundant, metachromatic, cytoplasmic granules characteristic of mast cells. A small cluster of normal hepatocytes is seen at the bottom center of the photomicrograph. (Wright-Giemsa, original magnification $\times 125$)

Figure 17—Hemangiosarcoma cells have a spindle-shaped, wispy, veil-like cytoplasm that often contains small, clear cytoplasmic vacuoles. Several malignant features such as high nuclear:cytoplasmic ratio, large prominent nucleoli, and a coarsely clumped chromatin pattern are present. (Wright-Giemsa, original magnification $\times 250$)
topoietic cells that originates in bone marrow. However, the liver and spleen are frequent sites of metastasis. Diffuse hepatomegaly may result, and blast cells of the lymphoid, myeloid, or erythroid cell lines may be encountered.

**SUMMARY**

In conclusion, we believe that cytologic evaluation of the liver is a simple technique that is very useful in the diagnosis of many hepatic disorders in dogs and cats. We recommend that liver cytology be routinely used to confirm or support a clinically based diagnosis. Combining cytopathologic findings with laboratory findings provides valuable information regarding the nature of many liver disorders affecting dogs and cats. If cytopathologic findings are inconclusive, a biopsy sample for histopathologic examination is warranted.

**REFERENCES**


**ARTICLE #4 CE TEST**

The article you have read qualifies for 1.5 contact hours of Continuing Education Credit from the Auburn University College of Veterinary Medicine. Choose the best answer to each of the following questions; then mark your answers on the postage-paid envelope inserted in *Compendium*.

1. In dogs and cats, the presence of indistinct cytoplasmic vacuolation and peripheral cytoplasmic clearing is most consistent with accumulation of a. glycogen. d. all of the above b. lipid. e. none of the above c. bile pigment.
2. Glycogen accumulation can be associated with which condition(s)? a. steroid hepatopathy b. nodular hyperplasia c. idiopathic vacuolar degeneration d. Cushing’s syndrome e. all of the above
3. Definitive confirmation of lipid vacuolar change is made based on which special stain? a. Oil red O b. Luxol fast blue c. periodic acid–Schiff d. Wright-Giemsa e. none of the above
4. Cytologically, normal hepatocytes appear as a. sheets of cuboidal epithelium. b. clusters of columnar epithelium. c. binuclear nuclei with multiple nucleoli. d. uniform cells with a single prominent nucleolus. e. large cells with a very high nuclear:cytoplasmic ratio.
5. Which statement regarding HCCs is false? a. HCCs can be noted in any lobe of the liver. b. HCCs are divided into nodular, diffuse, and massive forms. c. Massive forms usually have a lower metastatic potential than other forms. d. Biologic behavior is the same for all forms. e. HCCs have similar biologic behavior in cats and dogs.
6. In a fine-needle aspirate of feline liver, clusters of hepatocytes in which the cytoplasm contains abundant, clear, punctate vacuoles is most consistent with which liver disease(s)? a. hepatic lipidosis
b. hepatic lymphoma
c. lymphocytic portal hepatitis
d. Vacuoles are normal in feline hepatocytes.
e. none of the above

7. Which statement regarding inflammatory liver disease in dogs and cats is false?
a. Cytologic identification of inflammatory disease is difficult because of large amounts of blood contamination.
b. Cytologic identification of inflammatory disease is difficult because of the focal nature of the inflammatory lesion.
c. Inflammatory lesions are usually periductular in location.
d. Absence of inflammation on cytology can rule out an inflammatory disease.
e. Cytology is as sensitive as histology for the evaluation of inflammatory disease.

8. The presence of clumps of amorphous basophilic material, usually in the shape of cellular cytoplasm, is indicative of
a. hepatocellular regeneration.
b. vacuolar change.
c. necrosis.
d. hydropic degeneration.
e. Cushing's disease.

9. The inability to _______________ is a limitation of cytologic evaluation of the liver.
a. identify degenerative changes
b. identify neoplastic conditions
c. identify cholestasis
d. consistently identify focal inflammatory disease

e. identify hepatic lipidosis

10. Cytologic findings for a liver aspirate collected from a 10-year-old dog revealed moderate vacuolar degeneration with peripheral cytoplasmic clearing, small amounts of bile pigment, and mild extramedullary hematopoiesis. Ultrasonography of the liver showed several small hepatic nodules. Biochemical changes included mild increases in alanine aminotransferase and aspartate aminotransferase activities. What is the diagnosis based on biochemical, ultrasonographic, and cytologic findings?
a. hepatic carcinoma
b. hepatocellular regeneration
c. nodular hepatic hyperplasia
d. hepatic inflammatory disease
e. none of the above