Effusion Cytology

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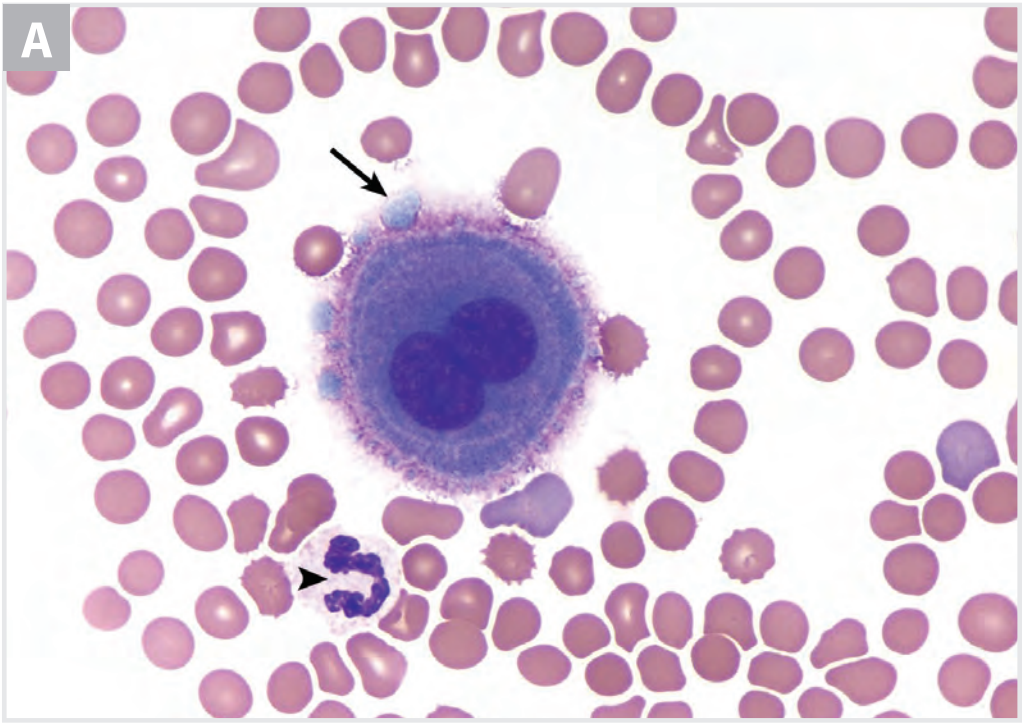
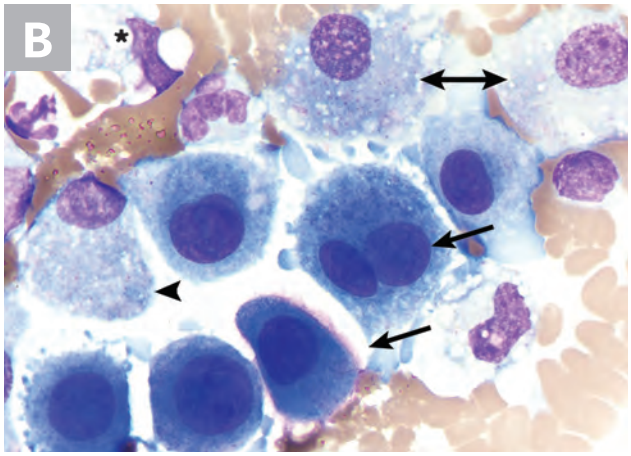
Effusions result from increased hydrostatic pressure or vascular permeability, altered oncotic pressure, or impaired lymphatic drainage. Effusions into body cavities (eg, thorax, abdomen, pericardial sac) are most commonly associated with inflammation, neoplasia, hemorrhage, trauma, obstruction, or leakage from the urinary or biliary tracts. Effusion cytology is relatively noninvasive and inexpensive and often provides an accurate diagnosis or contributes to diagnostic planning and prognosis.

Clinical history and physical examination findings are helpful in establishing differential diagnoses. For example, a young cat with weight loss and hyperproteinemia is more likely to have an inflammatory effusion from FIP than from a neoplastic process. Likewise, an older large-breed dog with acute collapse and a large splenic mass is more likely to have hemorrhagic effusion from a ruptured hemangiosarcoma than from a transudate associated with hyperadrenocorticism.

Typically, only several milliliters of fluid are present in the thorax, abdomen, and pericardial sac in dogs and cats. The fluid is clear, colorless, and minimally cellular ($<3 \times 10^9$ cells/L) with a relatively low total protein concentration (<2.5 g/dL).[1] There is some variability in classifying effusions, and several schemes and algorithms are presented in the literature.[1,2] Recent classification schemes have simplified effusion categories into low-protein transudates (<2.5 g protein/dL and $<3 \times 10^9$ nucleated cells/L), high-protein transudates (≥2.5 g protein/dL and $<3 \times 10^9$ nucleated cells/L), and exudates (≥2.5 g protein/dL and $\geq 3 \times 10^9$ nucleated cells/L).[1] A hemorrhagic effusion is suggested if the fluid packed cell volume is ≥25% that of the peripheral blood or if $>0.5 \times 10^{12}$ RBCs/L are present.[1,3] Neoplastic processes can be associated with any fluid type, emphasizing the importance of microscopic evaluation.

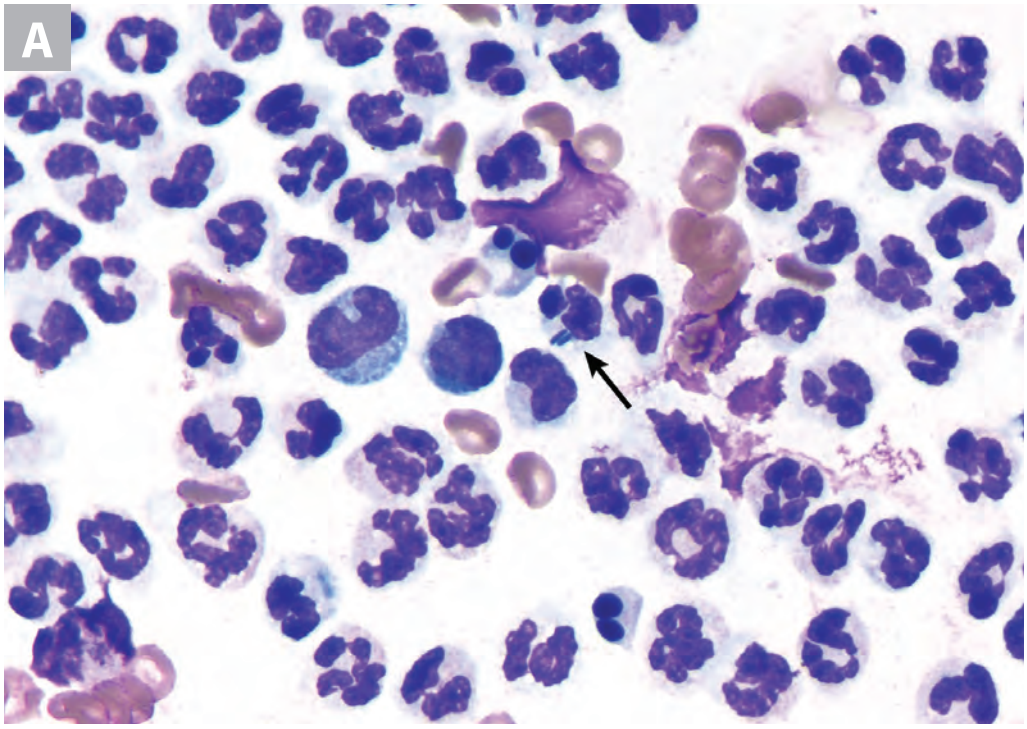
Examples of the types of cells that occur in effusions are included in this image gallery.





▸ **FIGURE 1** Mesothelial cells. Thoracic fluid from a dog (***A***). Body cavities are lined by mesothelial cells, which are present in variable numbers in most effusions. Mesothelial cells (***arrow***) are much larger than neutrophils (***arrowhead***) and are characterized by abundant basophilic cytoplasm that often has an eosinophilic fringe border or corona. The cytoplasmic blebs seen along the upper left border of the cell (***tip of arrow***) likely are an artifact. Round, central nuclei have stippled chromatin and may have visible nucleoli. Binucleated cells are not uncommon. *Wright-Giemsa stain; magnification 1000×*

Pericardial fluid from a dog (***B***). Several large reactive mesothelial cells with deeply basophilic cytoplasm are apparent in the center (***arrows***). Reactive mesothelial cells occur with inflammation or fluid accumulation from other causes and are characterized by increased variation in cell size, nuclear size, and nuclear:cytoplasmic ratio, as well as increased numbers of binucleated and multinucleated cells. These features are common in pericardial fluid from varying causes and are similar to those of neoplastic epithelial cells, which may be difficult to differentiate from reactive mesothelial cells based only on morphology. In addition, there are several macrophages with foamy cytoplasm (***arrowhead*** and ***double-sided arrow***), one with erythrophagocytosis (***asterisk***), and several neutrophils, likely from blood contamination. *Wright-Giemsa stain; magnification 1000×*



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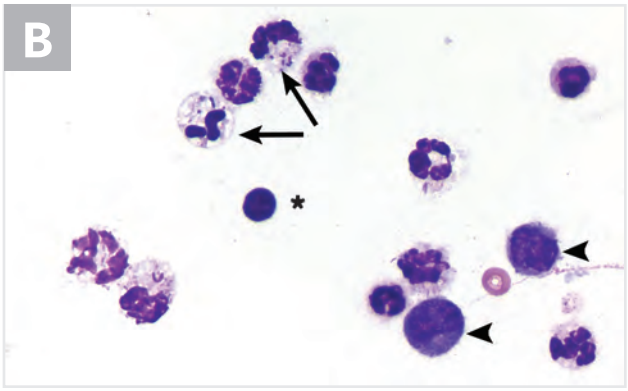
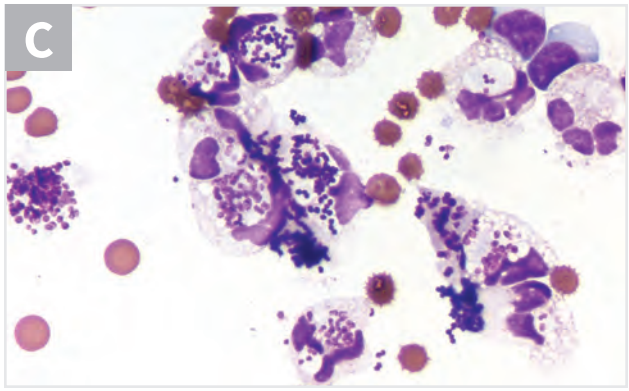
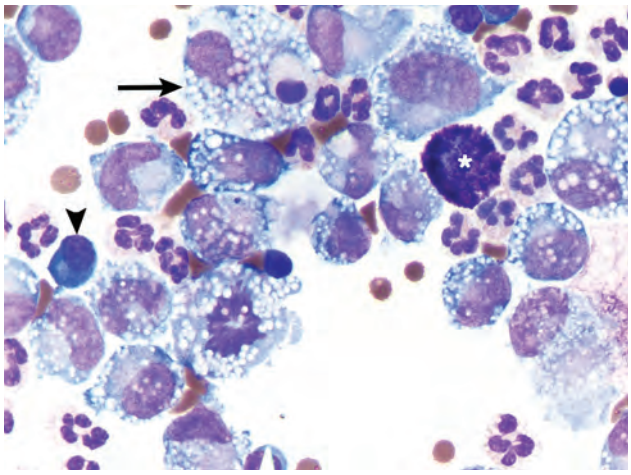




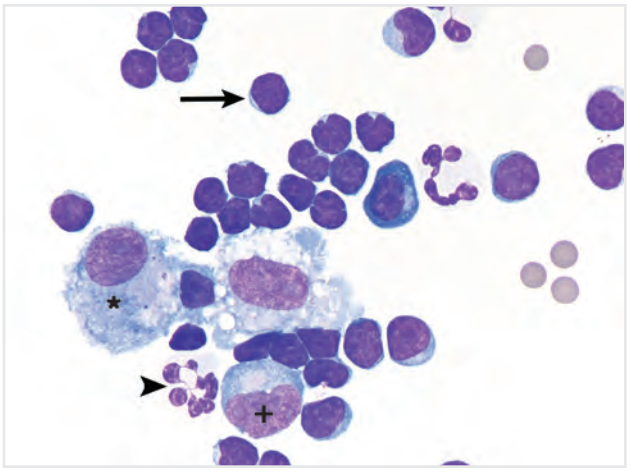
▲ **FIGURE 2** Neutrophilic inflammation. Thoracic fluid from a dog (***A***). Neutrophils may be present in many types of effusions, including transudates, and are useful for size comparison with other cells. Increased numbers of neutrophils occur with inflammation, which can be septic or nonseptic. Nondegenerate neutrophils, as shown here, have distinct nuclear borders and tightly clumped chromatin. Although the neutrophils appear nondegenerate in this effusion, 2 large, dark blue bacterial rods may be seen in one neutrophil (***arrow***). It is more typical for neutrophils to appear degenerate with bacterial infection, as shown in ***Figure B***. The absence of bacteria on cytology does not preclude the presence of infection, as cytology is not as sensitive as culture. *Wright-Giemsa stain; magnification 1000×*

Abdominal fluid from a dog (***B***). Degenerate neutrophils often occur with bacterial infection and are characterized by swollen nuclei with less-condensed chromatin and vacuolated cytoplasm. Two neutrophils are present with intracellular bacterial rods and cocci (***arrows***). A small lymphocyte (***asterisk***) and 2 large mononuclear cells (***arrowheads***) are present. *Wright-Giemsa stain; magnification 1000×*

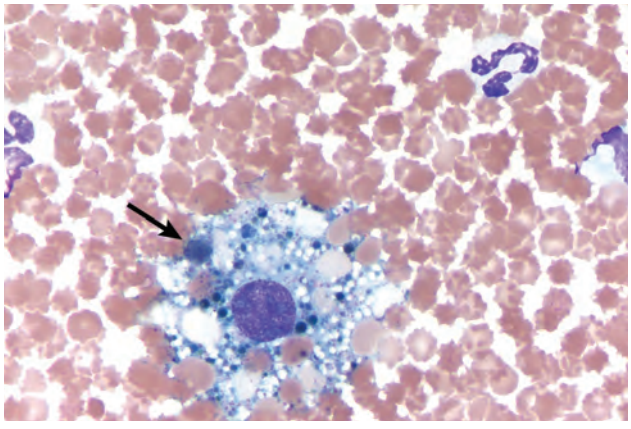
Abdominal fluid from a dog (***C***). Bacteria typically stain dark blue with Romanowsky stains, as seen in ***Figure A***. Most of the neutrophils in this image are severely degenerate and contain numerous large cocci. In some of the neutrophils, the cocci stain dark purple, whereas in others, the cocci appear swollen with lighter staining, likely from being metabolized in the neutrophil phagolysosome. *Wright-Giemsa stain; magnification 1000×*



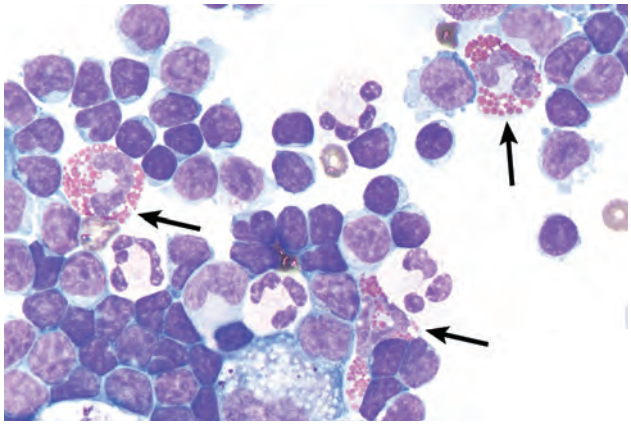
▲ **FIGURE 3** Abdominal fluid from a dog with chronic chylous effusion showing mixed inflammation. Macrophages are large, mononuclear cells that often have round, oval, or bean-shaped nuclei and abundant vacuolated cytoplasm. The vacuoles in this case likely are from imbibed lipid. Cytophagocytosis (***arrow***) is not uncommon, especially with inflammation, as shown in this mixed inflammatory effusion. A plasma cell, characterized by deeply basophilic cytoplasm with a perinuclear clear area and an eccentric round nucleus with condensed chromatin (***arrowhead***), can be seen. Plasma cells may be an indication of chronicity. A mast cell, characterized by numerous dark purple granules that obscure the nucleus, is also shown (***asterisk***). Mast cells can be part of the inflammatory response. *Wright-Giemsa stain; magnification 1000×*



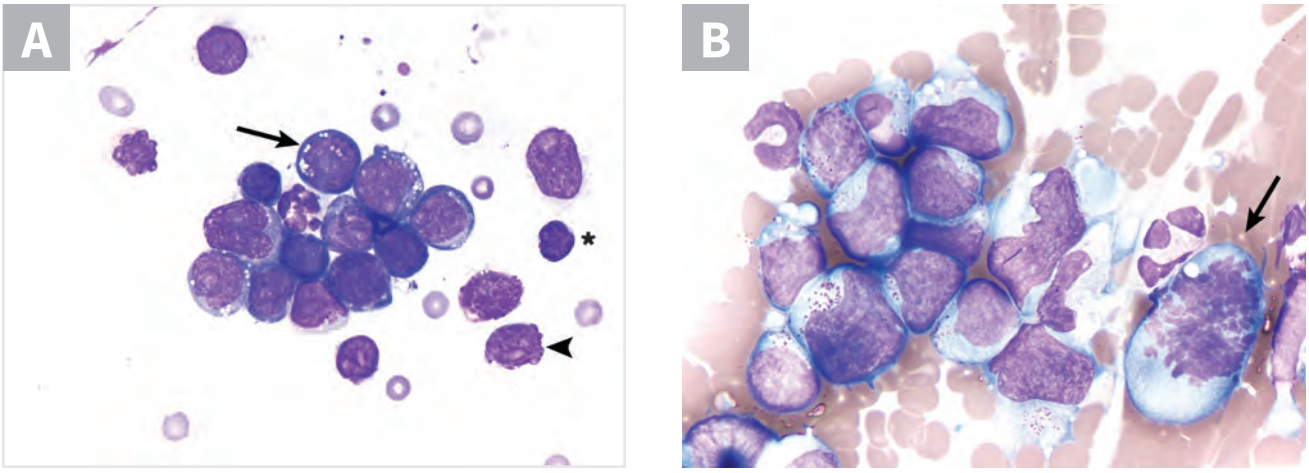
▲ **FIGURE 5** Thoracic fluid from a cat with chylous effusion. Numerous small lymphocytes (***arrow***), 3 neutrophils (***arrowhead***), 1 large mononuclear cell (***plus sign***), and 2 macrophages characterized by vacuolated cytoplasm (***asterisk***) can be seen. The small vacuoles are typical of phagocytosis of lipid in chylous effusions. The lymphocytes are smaller than the neutrophils, have round to slightly indented nuclei with condensed chromatin, and have a very high nuclear:cytoplasmic ratio, which is consistent with the well-differentiated lymphocytes typical of chylous effusion. This fluid appeared cloudy and white before and after centrifugation. A fluid triglyceride concentration of >100 mg/dL supports a diagnosis of chylous effusion.[4] *Wright-Giemsa stain; magnification 1000×*



▲ **FIGURE 4** Thoracic fluid from a dog with hemorrhagic effusion. RBCs can be present from blood contamination related to sample collection or from hemorrhage. With hemorrhage, macrophages phagocytize RBCs and metabolize hemoglobin to hemosiderin, which appears as a dark blue to greenish-black pigment in the cytoplasm of this macrophage (***arrow***). Erythrophagocytosis can occur with delayed sample processing, but hemosiderin would not be present. *Wright-Giemsa stain; magnification 1000×*

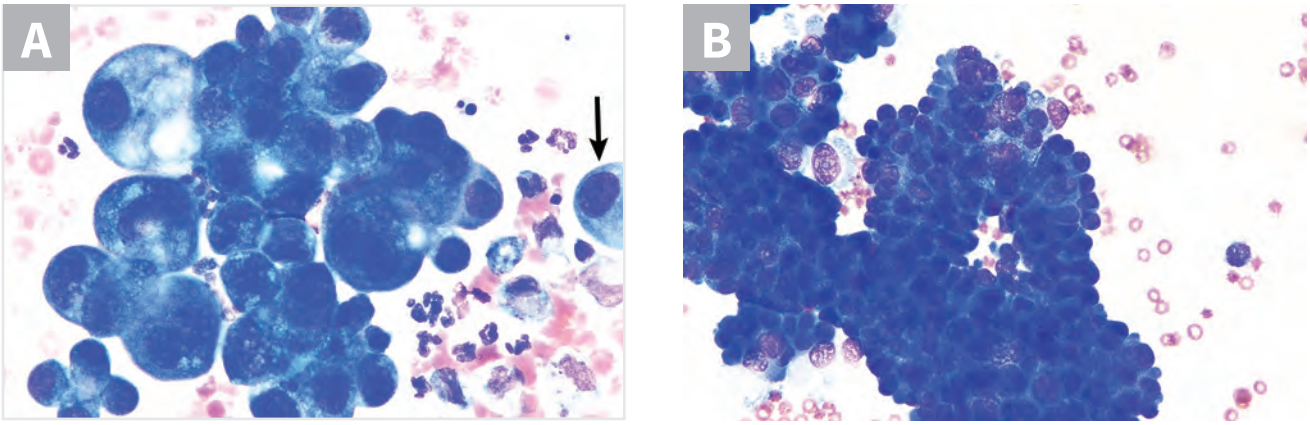


▲ **FIGURE 6** Thoracic fluid from a dog showing eosinophils. The distribution and morphology of the cells in this chylous effusion are similar to those in ***Figure 5***, except there are 3 eosinophils (***arrows***). The presence of eosinophils can be relatively nonspecific, and numbers can be variable. They can occur as part of an idiopathic hypereosinophilic syndrome or with parasites; allergic, hypersensitivity, or foreign body reactions; inflammation; neoplasia (mast cell tumor or lymphoma); heart failure; or protein-losing enteropathy. *Wright-Giemsa stain; magnification 1000×*



▲ **FIGURE 7** Thoracic effusion in a cat with lymphoma (***A***). Most of the lymphocytes are larger than the neutrophil in the center. These large lymphocytes (***arrow***) have moderate amounts of basophilic cytoplasm and large, round to slightly irregular nuclei with fine chromatin and 1-2 prominent nucleoli and are consistent with a diagnosis of lymphoma. The small vacuoles in the neoplastic lymphocytes most likely resulted from the fluid environment. Bare nuclei from broken cells (***arrowhead***) should not be evaluated because they may be misinterpreted as neoplastic lymphocytes. A normal small lymphocyte (***asterisk***) appears smaller than the neoplastic lymphocytes. *Wright-Giemsa stain; magnification 1000×*

Abdominal fluid from a dog with lymphoma (***B***). Most of the cells are large lymphocytes with moderate amounts of lightly basophilic cytoplasm that often contains foal areas with magenta granules. Nuclei are round to irregular-shaped and have smooth chromatin and indistinct nucleoli. These cells are consistent with a neoplastic proliferation of large granular lymphocytes, which are cytotoxic T lymphocytes. There is also a mitotic figure (***arrow***). *Wright-Giemsa stain; magnification 1000×*



▲ **FIGURE 8** Thoracic effusion from a dog with carcinoma (***A***). These large clusters of cohesive, atypical cells exhibit marked anisocytosis and anisokaryosis. The chromatin is fine to granular, and there are prominent nucleoli (***arrow***). These cells are much larger as compared with the nondegenerate neutrophils and erythrocytes present in the background. *Wright-Giemsa stain; magnification 500×*

Thoracic fluid from a dog with mesothelioma (***B***). The large clusters have a frond- or papillary-like appearance. Anisocytosis and anisokaryosis are relatively mild in this case; however, some mesotheliomas can exhibit marked atypia. The chromatin is stippled to coarse, and prominent nucleoli may be present but are not apparent at this magnification. Neoplastic effusions can be highly cellular due to shedding of neoplastic cells into the effusion or from an accompanying inflammatory response. It can be difficult to distinguish carcinoma from highly reactive mesothelial cells or mesothelioma based on cytology. A biopsy is often needed for confirmation, along with special staining. *Wright-Giemsa stain; magnification 500×*

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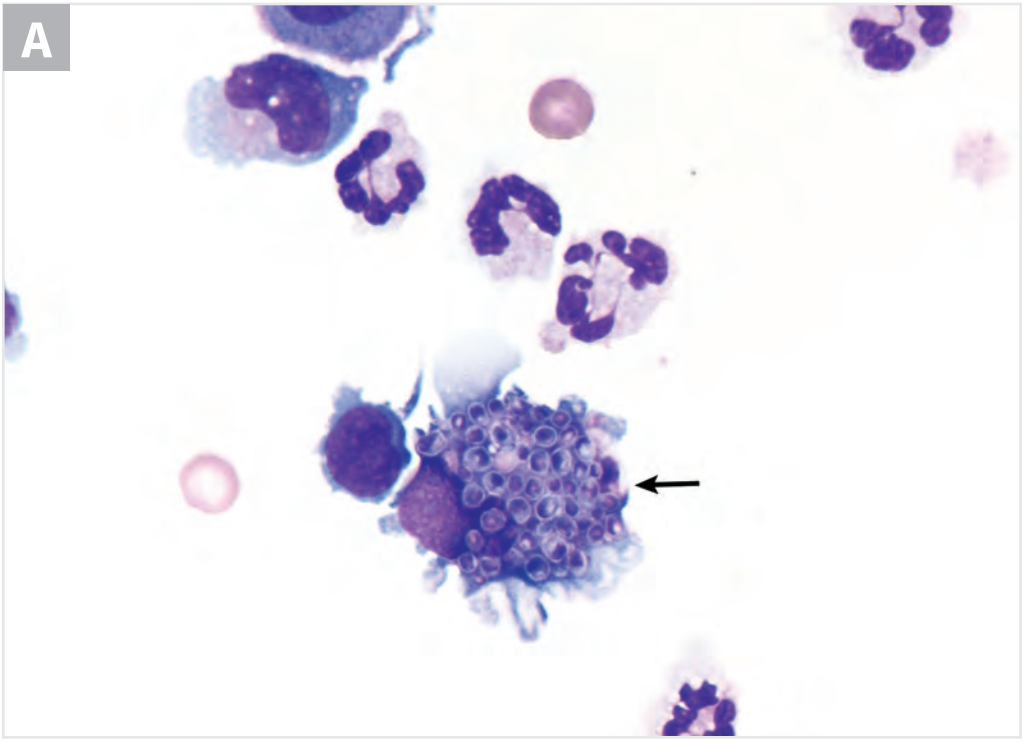
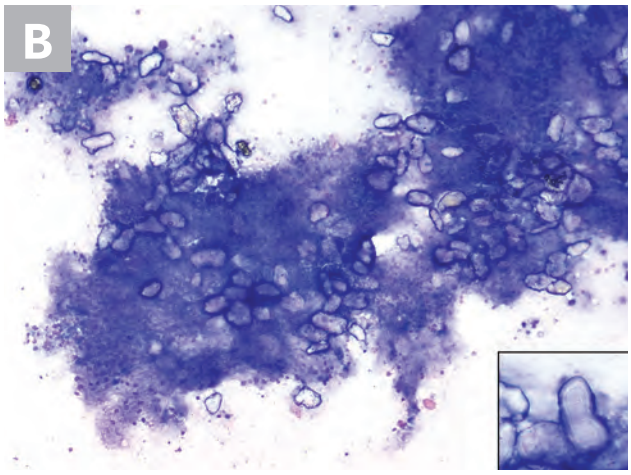
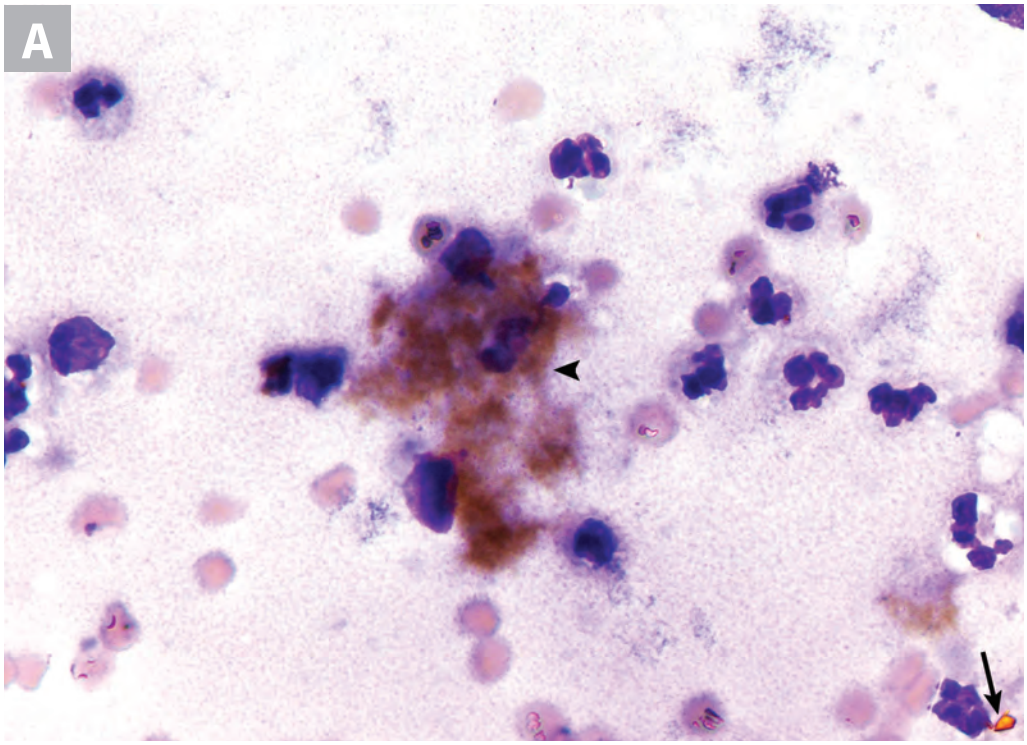




▲ **FIGURE 9** Infectious organisms. Abdominal fluid from a dog with histoplasmosis (***A***). The macrophage (***arrow***) contains numerous fungal organisms compatible with *Histoplasma capsulatum*. These organisms are 1 to 4 µm in diameter with a purple-staining nucleus and a clear, capsule-like rim. Five nondegenerate neutrophils, 1 small lymphocyte, and 1 large mononuclear cell are present. Fungal organisms can occasionally be observed in effusions as extensions of systemic disease (eg, *Histoplasma* spp, *Blastomyces* spp, *Coccidioides* spp, *Cryptococcus* spp infection) or from leakage of gut contents (eg, *Candida* spp infection). *Wright-Giemsa stain; magnification 1000×*

Abdominal fluid from a dog with peritoneal cestodiasis that contains cellular debris and calcareous corpuscles from the larvae of the *Mesocestoides* spp tapeworm (***B***). Calcareous corpuscles are 20 to 30 µm in diameter calcified granules that can be clear to light yellow. *Wright-Giemsa stain, magnification 200×*. A higher magnification (***inset***) shows the concentric rings that may be apparent in the calcareous corpuscles.



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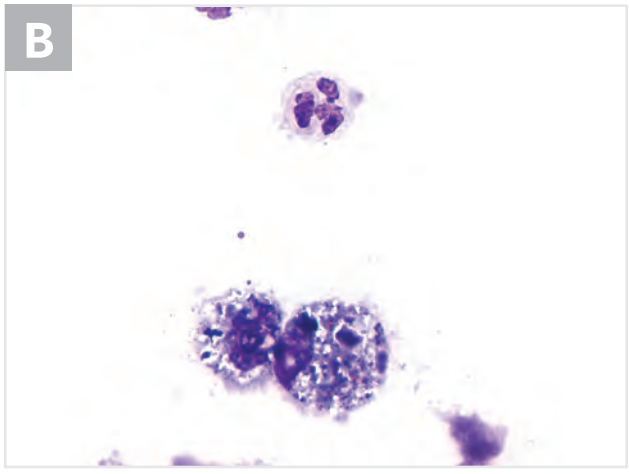
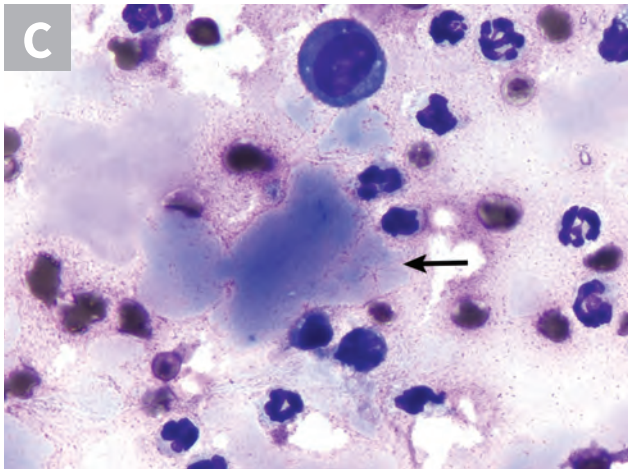
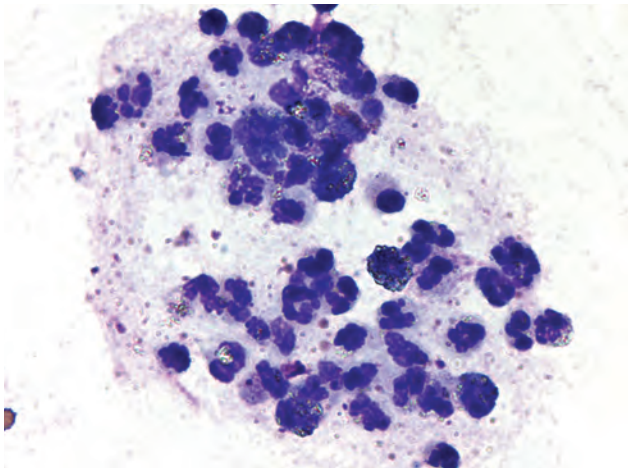




▲ **FIGURE 10** Bile peritonitis. Abdominal fluid from a dog with bile peritonitis from a ruptured gallbladder (***A***). Many neutrophils are present, and there is a grainy, proteinaceous-appearing background. Extracellular, amorphous, orange/yellow bile pigment is present (***arrowhead***), and a bilirubin crystal is seen in the lower right corner (***arrow***). *Wright-Giemsa stain; magnification 1000×*

Abdominal fluid from a dog (***B***). When phagocytized by macrophages, bile pigment can appear blue or black in color and may be difficult to distinguish from hemosiderin. *Wright-Giemsa stain; magnification 1000×*

Abdominal fluid from a dog (***C***). In this case of white bile peritonitis, there is amorphous blue to pink extracellular material that lacks the typical yellow bile staining (***arrow***). Because bile is irritating, neutrophilic inflammation is apparent. In both typical bile peritonitis and white bile peritonitis, the abdominal fluid bilirubin concentration is often 2-fold greater than serum bilirubin,[5] which may aid in diagnosis. *Wright-Giemsa stain; magnification 1000×*



▲ **FIGURE 11** Peritonitis with barium. There are many degenerate and nondegenerate neutrophils in a granular, proteinaceous-appearing background. Barium that leaked from the intestinal tract during a contrast study is apparent as clear to pale yellow, intracellular and extracellular crystalline material. Inflammation results from the irritating nature of the contrast material as well as from leakage of organisms from the intestinal tract. *Wright-Giemsa stain; magnification 1000×*

References

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