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Lymph node cytology

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Lymph node cytology is quick, easy, and rewarding. Cytologic samples of peripheral and/or internal lymph nodes may be collected by fine-needle aspiration biopsy (FNAB) or nonaspiration fine-needle biopsy techniques. In addition, imprints or scrapings may be made from lymph nodes that have been surgically removed or at necropsy.

Lymph node cytology is an excellent way to evaluate a lymphadenopathy whether it is a single node enlarged, multiple nodes enlarged, or a generalized lymphadenopathy. If multiple lymph nodes are enlarged, more than one should be sampled. A lymph node away from the mouth or any site of inflammation should be aspirated as well as any lymph node close to a site of inflammation. Generally, if no lymph nodes are enlarged, lymph node cytology is not helpful.

The lymph nodes generally palpated in dogs and cats include the submandibular, prescapular, and popliteal lymph nodes. For peripheral lymph nodes, cytologic collection can be performed within a few minutes with little or no risk to the patient. When interpreted by the attending clinician, lymph node cytology saves time, allows for early implementation of appropriate therapy, and decreases owner anxiety by providing answers quickly.

Because lymph nodes typically exfoliate high numbers of cells, smears are often diagnostic of either a process or a disease condition that can be either primary or secondary in nature. Common causes of lymphadenopathy include neoplasia (lymphosarcoma and metastatic neoplasia), hyperplasia or reactive lymphadenopathy, lymphadenitis (neutrophilic, purulent, eosinophilic, pyogranulomatous, or granulomatous), immune stimulation, and extramedullary hematopoiesis. It is important to remember that these

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classifications are not mutually exclusive and that more than one condition may be occurring in the same node.

Sample collection and preparation

Fine-needle aspiration biopsy

For cutaneous lymph nodes, the skin over the node to be aspirated needs no special preparation. It is prepared as one would prepare the skin for giving an injection. A small-gauge needle (25–21 gauge) is affixed to a 5-mL or larger syringe. The node to be aspirated is stabilized between the thumb and forefinger, and the needle is inserted into the node. A vacuum of about three quarters of the syringe volume is placed on the needle by rapidly withdrawing the plunger. If the node is large enough and the animal is calm enough, the needle is redirected two or three times within the node while sustaining the vacuum. During redirection of the needle, care should be taken not to withdraw the needle from the lymph node. The vacuum is then released. When the vacuum is fully released, the needle is withdrawn from the node and skin. If the node is only slightly enlarged or if the animal is difficult to restrain, the needle is inserted into the node and negative pressure is applied and released before the needle is redirected. Also, anytime blood appears in the hub of the needle, aspiration of that area should cease. After the node has been aspirated and the needle withdrawn from the node and skin, the needle should be removed from the syringe. Air is then drawn into the syringe, and the needle is replaced onto the syringe. The point of the needle is then positioned close to the frosted end of a microscope slide, and the syringe plunger is depressed, moving air through the needle and forcing the aspirated material onto the microscope slide in a spray of approximately 0.5 cm in diameter. Often, more preparations can be made by repeating the expulsion procedure. If not, additional aspirations should be collected. Also, if multiple nodes are enlarged, more than one node should be aspirated. Once the aspirate has been collected and forced onto a glass slide, it needs to be spread into a monolayer without causing excessive cell rupturing. The collected material needs to spread soon after collection so that it does not start to dry out. Multiple techniques for smear preparation are described in another article in the November 2002 issue of *Veterinary Clinics of North America: Small Animal Practice* [1]. For lymph nodes, however, two major techniques (blood smear and squash preparation) are used. In the blood smear technique, the aspirated material is spread by pulling a slanted microscope slide into the aspirate spray (much like you would prepare a blood smear) and then pulling the slanted slide rapidly forward (as you would in preparing a blood smear). This technique has minimal shearing forces and causes minimal cell rupturing. It is the preferred technique if sufficient blood and tissue fluid are present in the aspirate to allow its use. Otherwise, a squash preparation technique is generally used. To make a squash preparation, a microscope slide is placed over

the aspirate spray and slid across it. After the smears are prepared, they are air dried and stained with any hematologic stain (eg, Diff-Quik, Wright's stain, Dade-Behring, Inc., Deerfield, IL) as described in the November 2002 issue of *Veterinary Clinics of North America: Small Animal Practice* [1].

Nonaspiration fine-needle biopsy

A nonaspiration technique can be used to collect lymph node samples. It is briefly described here but is described more fully in the November 2002 issue of *Veterinary Clinics of North America: Small Animal Practice* [1]. The procedure is performed by placing a small-gauge needle onto a syringe and prefilling the syringe with air. The node to be aspirated is stabilized as described previously. The syringe and needle are held as if holding a pencil or a throwing dart. The needle is inserted into the node and, using a stabbing motion, is quickly inserted (stabbed) into the node several times along the same plane, being careful not to exit the node during the collection. Cells are collected in the needle bore by capillary action on the cell/fluid slurry created during the stabbing. The needle is withdrawn, and the material is expelled onto a glass slide by rapidly depressing the plunger. Smears are made as described previously. Generally, material sufficient for only one smear is collected, so multiple collections are needed.

Imprints (touch preparations)

Lymph node imprints may be prepared if the lymph node has been excised. First, the lymph node is cut, and the cut surface is blotted with an absorbent paper. The cut surface is then gently pressed against the flat surface of a microscope slide and lifted straight up. Care should be taken not to rotate or drag the lymph node surface against the surface of the microscope slide. Rotating or dragging the lymph node surface against the microscope slide can result in cell rupture. The imprint smears are then air dried and stained with a hematologic stain.

Scrapings

Like imprints, scraping can be prepared if the lymph node has been excised. The excised lymph node is cut, and the cut surface is blotted. The cut surface is then scraped using the edge of a microscope slide or other blunt instrument. The material scraped from the cut surface is then smeared onto the flat surface of another microscope slide, and the smear is air dried.

Staining

The air-dried smears are stained with any of the routine hematologic stains (eg, Wright's, Diff-Quik). More information on staining is provided in the November 2002 issue of *Veterinary Clinics of North America: Small Animal Practice* [1].

Lymph node cell types

Cells found in lymph node cytology preparations include small lymphocytes, medium-sized lymphocytes, large lymphocytes, plasma cells, macrophages, mast cells, neutrophils, eosinophils, inflammatory giant cells, and metastatic cancer cells.

Small lymphocytes

Small lymphocytes are 7 to 10 μm in diameter, are smaller than a neutrophil, and have no visible nucleolus (Fig. 1). Small lymphocytes make up greater than 75% (75%–95%) of the lymphocytes in a normal lymph node. Small lymphocytes have a scanty amount of clear to light blue cytoplasm that is often only visible in a small area because it runs confluent with the nucleus for most of its course around the nucleus. The nucleus is roundish to oval but indented. It has dense clumps of light and dark chromatin (euchromatin and heterochromatin) forming a coarsely smudged pattern. Care should be taken to not confuse the dense clumps of heterochromatin with a nucleolus.

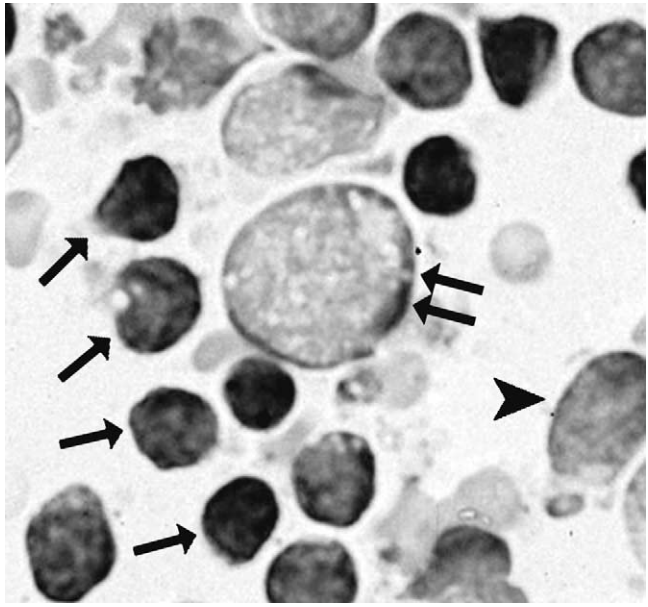

Fig. 1. Aspirate from a hyperplastic lymph node. Numerous small lymphocytes (*arrows*) are present. A lymphoblast (*double arrows*) and prolymphocyte (*arrowhead*) are present also. Numerous lymphoglandular bodies are present in the background of the smear. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

Medium lymphocytes

Medium-sized lymphocytes (also called prolymphocytes) are approximately 9 to 15 μm in diameter, are about the same size as a neutrophil, have a visible nucleolus, and make up about 5% to 15% of the lymphocytes in a normal lymph node (see Fig. 1). They have a moderate amount of bluish cytoplasm that occasionally contains a few azurophilic granules. The nucleus is round to oval, with a stippled to granular chromatin pattern, and often has a single prominent nucleolus. Nucleoli are not always prominent in prolymphocytes; some prolymphocytes may have indistinct nucleoli, and nucleoli may not be visible in some cells.

Lymphoblasts (large lymphocytes)

Large lymphocytes (also called lymphoblasts) are generally greater than 15 μm in diameter, are larger than a neutrophil, have a visible nucleolus, and make up only about 5% of the lymphocytes in a normal lymph node (see Fig. 1). Lymphoblasts have a moderate amount of bluish cytoplasm that may appear granular because of the dark-staining protein-rich areas and lighter staining areas of some organelles. Some lymphoblasts may contain a few azurophilic granules. A clear area in the cytoplasm representing the Golgi apparatus may be visible. Nuclear shape is variable, ranging from roundish to irregular, and generally has a stippled chromatin pattern. Multiple nucleoli are often visible. Often, the cytoplasm tends to run confluent with the nucleus in one or more areas, making it not visible all the way around the nucleus.

Plasma cells

Plasma cells are medium-sized round to oval cells with a single eccentrically placed round nucleus (Fig. 2). Binucleate cells are common in plasma cell tumors but are not commonly seen in plasma cells present in immune-stimulated lymph nodes. The nuclear chromatin is coarsely clumped and may appear cordlike. Plasma cells have a moderate amount of deeply blue cytoplasm and generally have a visible Golgi apparatus appearing as a clear area located between the nucleus and greatest volume of cytoplasm. Occasionally, plasma cells are observed where the cytoplasm is filled with clear or pale blue-staining vacuoles that are actually packets of immunoglobulin. These cells are called Mott cells, and the vacuoles are called Russell bodies (Fig. 3) [2].

Mast cells

Mast cells are medium-sized round cells that have a round to oval nucleus, and the cytoplasm generally contains a moderate to high number of small reddish-purple (metachromatic) granules (see Fig. 2).

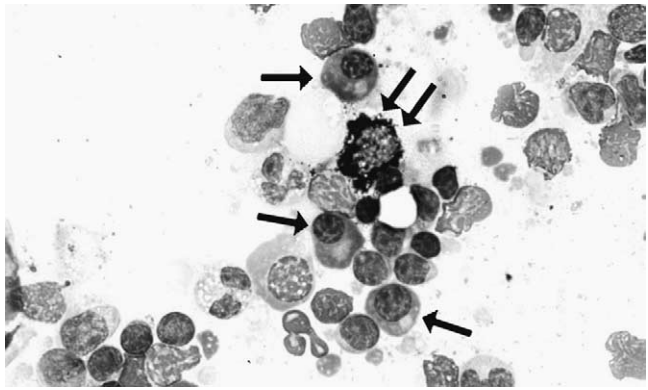

Fig. 2. Lymph node aspirate showing many small lymphocytes, plasma cells (*arrows*), and a mast cell (*double arrows*). (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

Neutrophils

Neutrophils in lymph nodes look like peripheral blood neutrophils. They have a segmented nucleus with coarsely clumped chromatin and a moderate amount of clear cytoplasm (Fig. 4).

Eosinophils

Eosinophils in lymph nodes look like peripheral blood eosinophils. Like neutrophils, eosinophils have a segmented nucleus with coarsely clumped chromatin. Eosinophils are larger than neutrophils, however, and their cyto-

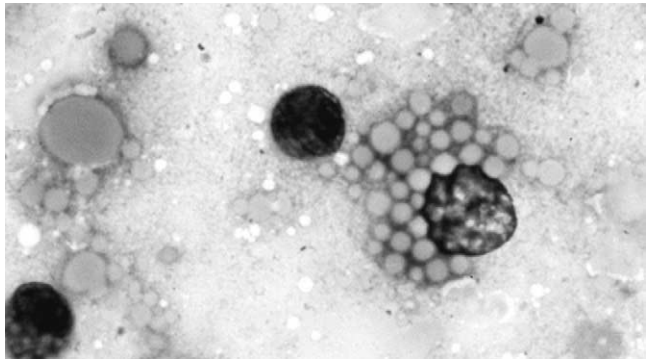

Fig. 3. Lymph node aspirate showing a Mott cell. Mott cells are plasma cells with their cytoplasm full of clear to blue-staining packets of immunoglobulin. The distinct packets of immunoglobulin are referred to as Russell bodies. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

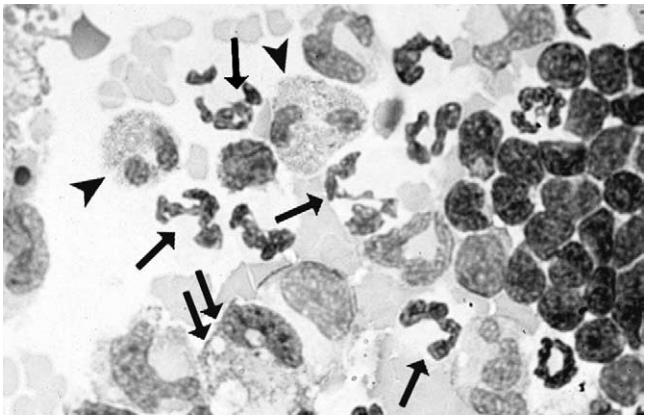

Fig. 4. Lymph node aspirate showing many small lymphocytes (right side of picture) and scattered neutrophils (*arrows*), macrophages (*double arrows*), and eosinophils (*arrowheads*). (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

plasm contains a few to many variably sized, roundish, red granules in dogs (see Fig. 4) and many small, rod-shaped, red granules in cats.

Macrophages

Macrophages are highly variable in size but tend to be large cells with abundant gray cytoplasm and a single round to oval to irregular nucleus with a lacy chromatin pattern. Often, the macrophages contain vacuoles (see Fig. 4) or phagocytic debris.

Inflammatory giant cells

Inflammatory giant cells occur when macrophages fuse. These cells indicate a granulomatous response and the presence of an agent that is difficult to phagocytize. These cells are large and multinucleated, have abundant blue-gray cytoplasm, and may contain phagocytized material.

Metastatic cancer cells

Neoplasia other than lymphoid neoplasia in a lymph node is considered metastatic. Metastatic neoplasia is identified by recognizing abnormally high numbers of a cell type that should be present in low numbers (eg, mast cell tumor) or by recognizing cell types that do not belong in a lymph node and have malignant criteria (eg, carcinoma cells). Metastatic tumor cells within lymph nodes are often carcinomas and adenocarcinomas and resemble the tumor of origin. Therefore, carcinoma and adenocarcinoma cells are

typically large cells (epithelial cells) that show moderate to marked criteria of malignancy (eg, anisokaryosis, anisocytosis, high nucleus-to-cytoplasm ratio, large angular nucleoli). Metastatic sarcomas are less common but do occur. Metastatic sarcoma cells generally appear as medium to large cells with tapered cytoplasm (cytoplasm tapers away from the nucleus in one or two directions) forming cytoplasmic tails in many of the cells. These cells show moderate to marked malignant criteria (a more complete description of malignant criteria is provided in the November 2002 issue of *Veterinary Clinics of North America: Small Animal Practice* [1]).

Interpretation

General

The proportion of the different types of lymphocytes (small, medium, and large) varies according to what process or processes are occurring (eg, immune stimulation, inflammation, neoplasia) in the lymph node. Knowledge of normal cytologic characteristics of lymph nodes helps the evaluator to recognize abnormal findings. In the nonneoplastic lymph node, lymphoblasts seldom make up more than 20% of the lymphoid cells, whereas in lymph nodes with lymphosarcoma, lymphoblasts typically make up more than 50% of the lymphoid cells. Figs. 5 through 7 are included to serve as an example of a decision-making tree for evaluating lymph node aspirates.

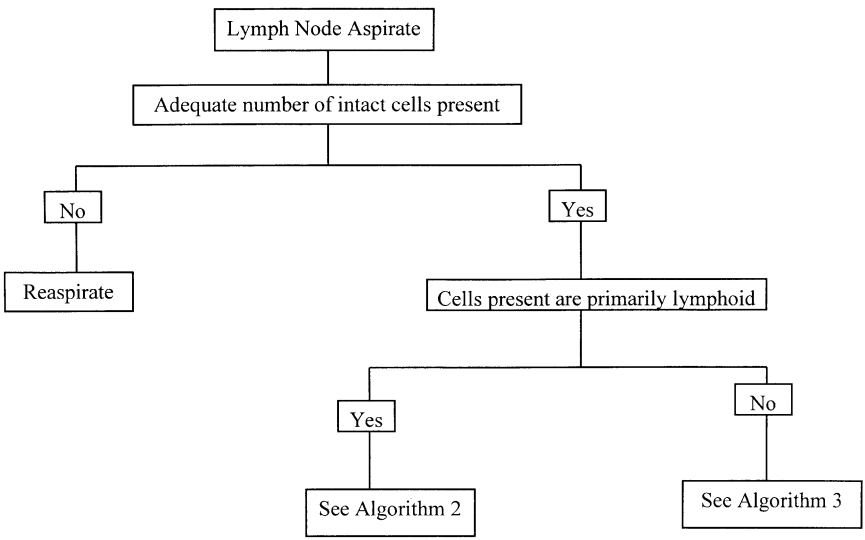

Fig. 5. Diagnostic approach to lymph node aspirates. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

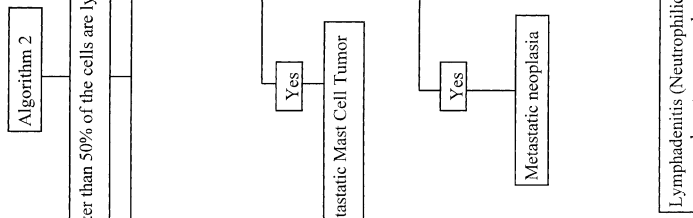

Fig. 6. Diagnostic approach to lymph node aspirates that consist primarily of lymphocytes. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

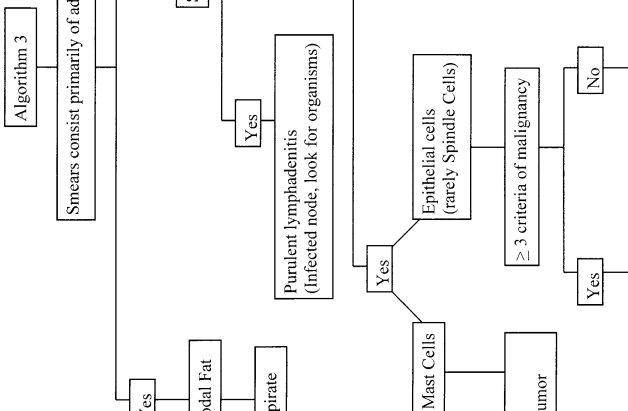

Fig. 7. Diagnostic approach to lymph node aspirates that do not consist primarily of lymphocytes. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

Normal lymph nodes

Normal lymph nodes consist primarily of small mature lymphocytes (75%–95% of all nucleated cells present) [2]. The remaining 5% to 25% of the cells are an admixture of the other various cell types but are primarily lymphoblasts and prolymphocytes, with lesser numbers of plasma cells and a few neutrophils and macrophages. Small cytoplasmic fragments shed from lymphoid cells are a common finding in all lymph node aspirates. These cytoplasmic fragments are called lymphoglandular bodies. It is important that these structures are not confused with or misidentified as an organism, parasite, or cell.

Lymphoma (lymphosarcoma)

Lymphoma may range from a generalized disease to a disease limited to a single node. Because lymph node architecture is lost with cytology, lymphoma is recognized on cytologic smears by the presence of abnormally increased numbers of lymphoblasts and/or prolymphocytes (greater than 50% of all nucleated cells present) (Figs. 8 and 9) [2]. Only intact nontraumatized lymphocytes should be evaluated cytologically. Some lymphocytes rupture or are traumatized during aspiration or slide preparation, causing them to spread out and appear larger than normal, which may make nucleoli become more visible. These ruptured or traumatized cells are usually easily recognized by their loose nuclear chromatin, which stains more eosinophilic than the nuclear chromatin of intact lymphocytes. Caution must be taken when evaluating smears with a high number of ruptured lymphocytes. Lymphoblasts are more fragile than small lymphocytes and tend to rupture more easily. Therefore, lymphosarcoma may be masked if a high number of

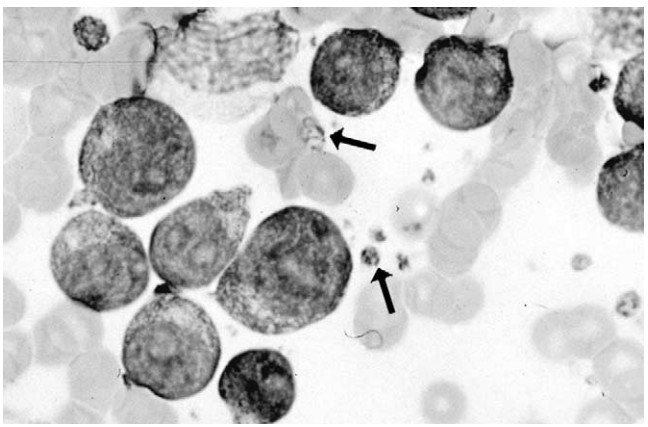

Fig. 8. Lymph node aspirate from a dog with lymphoma. Red blood cells, lymphoblasts, and lymphoglandular bodies (*arrows*) are shown. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

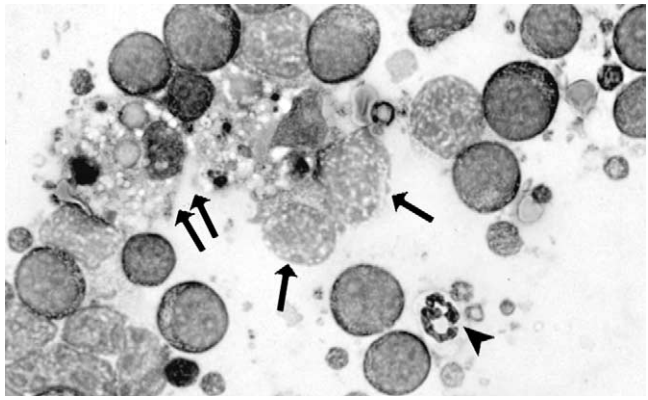

Fig. 9. Lymph node aspirate from a dog with lymphoma. Lymphoblasts greatly predominate on the smear. Ruptured cells (*arrows*), macrophages (*double arrows*), and a neutrophil (*arrowhead*) are present also. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

ruptured cells are present on the smear, causing the percentage of lymphoblasts to falsely decrease.

The higher the percentage of lymphoblasts and prolymphocytes, the surer one can be that lymphosarcoma is present. When these cells make up greater than 50% of all nucleated cells present, one can confidently make a diagnosis of lymphoma [2]. Lymph nodes with lymphoma usually have greater than 50% of their lymphoid cells as lymphoblasts, and greater than 80% of the cells are often lymphoblasts. Therefore, smears typically consist of a homogeneous population of large lymphoblasts (immature lymphocytes). Lymphoblasts have a small amount of basophilic cytoplasm that tends not to run all the way around the nucleus but travels confluent with the nucleus for part of its course. Lymphoblasts have a stippled (fine) nuclear chromatin pattern and often have multiple nucleoli. Morphologically, a neoplastic lymphoblast looks no different from a nonneoplastic lymphoblast. Therefore, it is the percentage of lymphoblasts and not malignant criteria (as with other neoplasias) that allows for the recognition of lymphoma. Fortunately, most lymphomas are lymphoblastic. Blastic lymphoid cells can be classified as centroblasts, immunoblasts, or lymphoblasts, for example, based on their morphology. At this time, treatment is not influenced by the different classifications, but it may be in the future. An excellent review of the different cell classifications is available elsewhere [3]. Immunophenotyping lymphomas into B- and T-cell types has been reported to aid in prognosis [3]. Also, cytoplasmic fragments (lymphoglandular bodies) are generally increased in all lymphomas but are not a reliable indication of neoplasia.

Rarely, lymphocytic lymphoma (small cell or well-differentiated lymphoma) occurs. These lymphomas yield only small lymphocytes and generally must be diagnosed by histopathology. The presence of only high numbers

of small lymphocytes (ie, the absence of the other cell types [lymphoblasts and prolymphocytes]) is suggestive of small cell lymphoma. When lymphoma is suspected but cannot be recognized cytologically, excisional biopsy of an affected lymph node should be performed. The entire node should be removed, incised at 0.25-inch intervals, and placed in 10% buffered formalin for histopathology. Histopathologic evaluation allows the pathologist to evaluate architecture, which is lost with cytology. If an impression smear or additional aspirates are made for cytologic evaluation, they should be submitted in a separate package from the formalin-fixed tissue, because formalin fumes "fix" the cells present on the cytology smear and interfere with their staining, making cytologic evaluation impossible.

Hyperplasia/reactive lymph nodes

Hyperplastic lymph nodes often appear cytologically similar to normal lymph nodes [4]. They are classified as hyperplastic (instead of normal) based on the history of an enlarged lymph node being aspirated. Hyperplastic lymph nodes consist of a marked predominance of small mature lymphocytes (Fig. 10). Reactive lymph nodes are similar to hyperplastic lymph nodes but have a greater number of other cell types present. Reactive lymph nodes have greater than 50% of their nucleated cells present as small mature lymphocytes with few to moderate numbers of prolymphocytes, lymphoblasts, and plasma cells (including Mott cells with Russell bodies). Mott cells are plasma cells that contain packets of immunoglobulin (Russell bodies). Hyperplastic/reactive lymph nodes represent lymphoid proliferation in response to antigenic stimulation. This can be localized (regional nodes draining an area of inflammation) or generalized (systemic antigenic stimulation as may occur with diseases like feline leukemia virus [FeLV], chronic

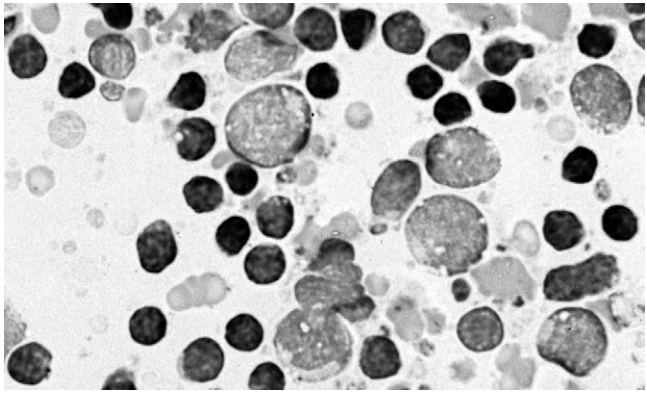

Fig. 10. Aspirate from a hyperplastic lymph node. Small lymphocytes greatly predominate. A few lymphoblasts and prolymphocytes are present also. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

ehrlichiosis, and Rocky Mountain Spotted Fever). If the antigenic stimulation is strong or if the lymph node is infected, lymphadenitis is the usual reaction.

Lymphadenitis

Lymphadenitis may be primary or secondary and result in neutrophilic, purulent, eosinophilic, pyogranulomatous, or granulomatous lymphadenitis, or a combination of these reactions may occur in the same or different nodes. With primary lymphadenitis, the node itself is infected. With lower bacteria, the lymph node(s) becomes heavily infiltrated with neutrophils, resulting in a purulent lymphadenitis and abscess formation, whereas higher bacteria like *Mycobacterium* often result in a granulomatous lymphadenitis. Mycotic infections are often pyogranulomatous but may sometimes be neutrophilic (eg, *Histoplasma capsulatum*). With secondary lymphadenitis, the node itself is not infected but is draining an inflamed area distant from the node. These nodes usually have neutrophilic and/or eosinophilic lymphadenitis. Increased numbers of plasma cells indicating immune stimulation are usually present with lymphadenitis of any cause. When lymphadenitis is present, a careful search for organisms and appropriate culturing should be performed.

Neutrophilic lymphadenitis

If five or more neutrophils are observed per 100× (oil-power) objective field, the lymph node is inflamed (Fig. 11). If 20% or greater of the cells are neutrophils, the inflammation can be classified as suppurative or purulent. Neutrophilic inflammation is commonly seen in nodes draining sites of inflammation. Infected nodes (bacterial) show purulent inflammation.

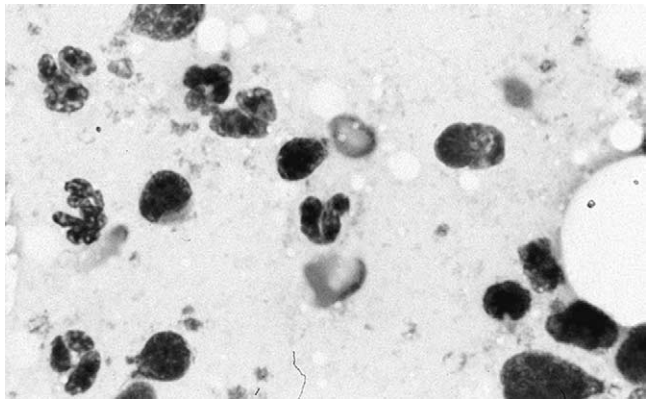

Fig. 11. Aspirate from a lymph node with neutrophilic lymphadenitis. Small lymphocytes and neutrophils are shown. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

Eosinophilic lymphadenitis

If three or more eosinophils are detected per 100× (oil-power) objective field, eosinophilic lymphadenitis is indicated (Fig. 12). The most common causes of eosinophilic lymphadenitis are dermatitis and parasitism.

Immune stimulation

If three or more plasma cells are detected per 100× (oil-power) objective field, immune stimulation is indicated. Immune stimulation is seen concurrently with inflammation in most instances.

Histiocytic (macrophagic or chronic) lymphadenitis

If five or more macrophages are detected per 100× (oil-power) objective field, a chronic inflammatory process should be suspected. Chronic inflammation can occur with neutrophilic or purulent inflammation. A thorough search for etiologic agents of histiocytic lymphadenitis (eg, fungal organisms, *Mycobacterium*) should be made (Figs. 13–15).

Granulomatous inflammation

If inflammatory giant cells are detected, a granulomatous inflammatory process is present. Granulomatous inflammation may occur concurrent with neutrophilic or purulent inflammation (pyogranulomatous). When granulomatous inflammation is detected, a thorough search for the cause of the inflammatory process (eg, fungal organisms) should be made.

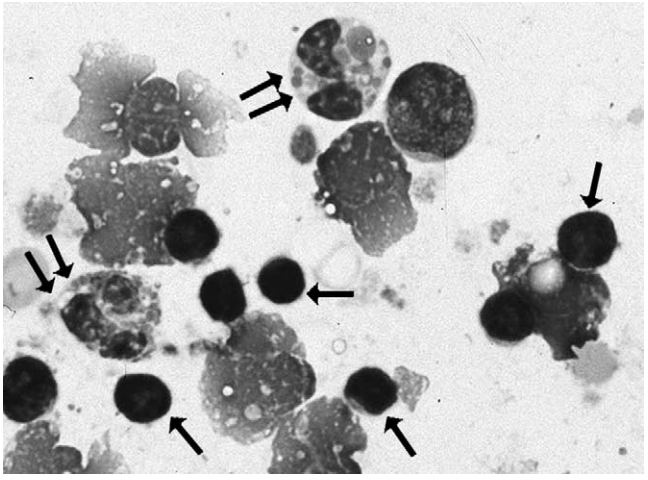

Fig. 12. Aspirate from a lymph node with eosinophilic lymphadenitis. Small lymphocytes (*arrows*) predominate, but eosinophils (*double arrows*) are present in increased numbers. Ruptured cells, red blood cells, and lymphoglandular bodies are present also. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

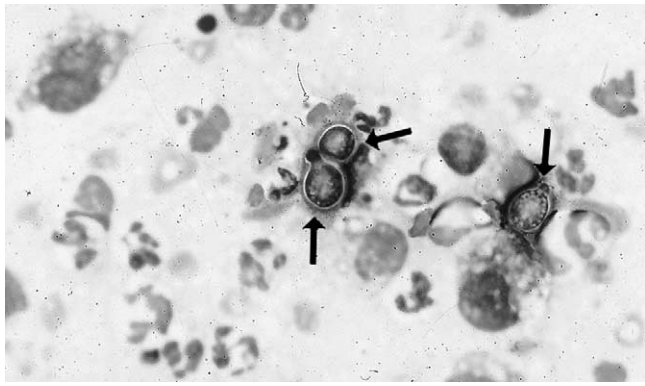

Fig. 13. Lymph node aspirate from a dog with blastomycosis. Neutrophils, macrophages, and *Blastomyces* organisms (*arrows*) are shown. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

Nonlymphoid neoplasia

FNAB has been shown to be highly sensitive and specific for evaluating regional lymph nodes for metastasis of solid tumors in dogs and cats [5]. In one study, cytologic evaluation of lymph node FNABs had a sensitivity of 100% and a specificity of 96% for detecting solid tumor metastasis to regional lymph nodes [5]. Metastatic cancer in a lymph node aspirate is documented if a cell type that should be present in low numbers is present in high numbers, such as mast cells (Figs. 16 and 17), or if cells that are foreign to the lymph node (eg, epithelial cells) are observed exhibiting three or more criteria of malignancy. Malignant epithelial cell tumors (carcinomas

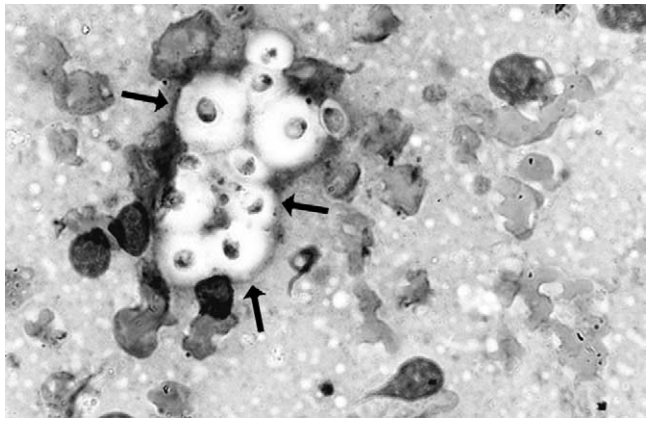

Fig. 14. Lymph node aspirate from a cat with cryptococcosis. Numerous *Cryptococcus* organisms (*arrows*) are present. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

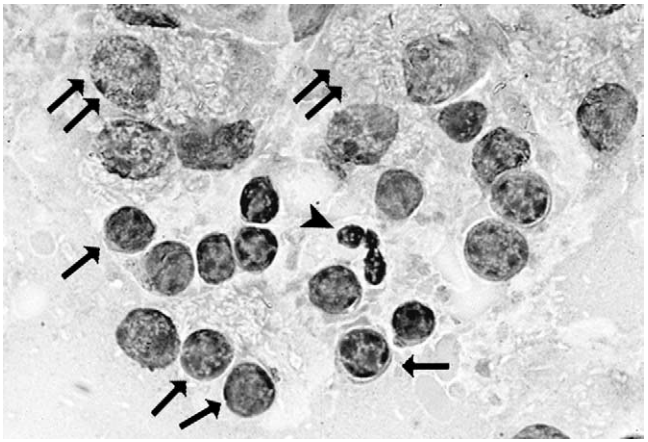

Fig. 15. Lymph node aspirate from an animal with generalized mycobacterial infection. Numerous small lymphocytes (*arrows*), scattered macrophages (*double arrows*), and a neutrophil (*arrowhead*) are shown. The macrophages contain many small negative images of bacterial rods. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

and adenocarcinoma) are the most frequently identified metastatic neoplasias. They appear as large (epithelial) cells in groups or clusters or individually and typically exhibit moderate to marked criteria of malignancy (Figs. 18–20). In addition, it is important to ensure that the aspirate was not taken from a normal organ other than the lymph node (eg, salivary gland).

Metastatic spindle cells (sarcomas) are observed less frequently than metastatic epithelial cells. Metastatic sarcomas typically appear as spindle

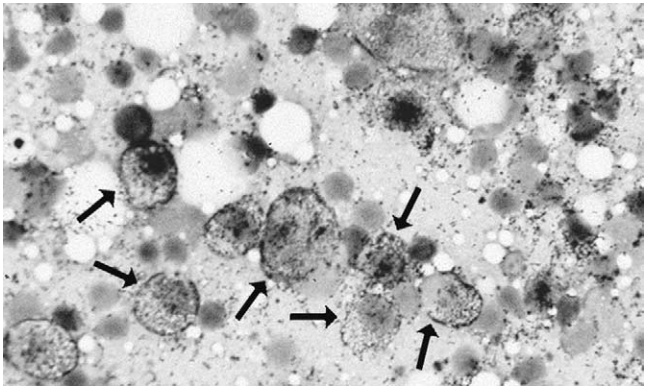

Fig. 16. Low-power view of a lymph node with metastatic mast cell tumor. Numerous mast cells (*arrows*) are present, and many mast cell granules are present free in the background. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

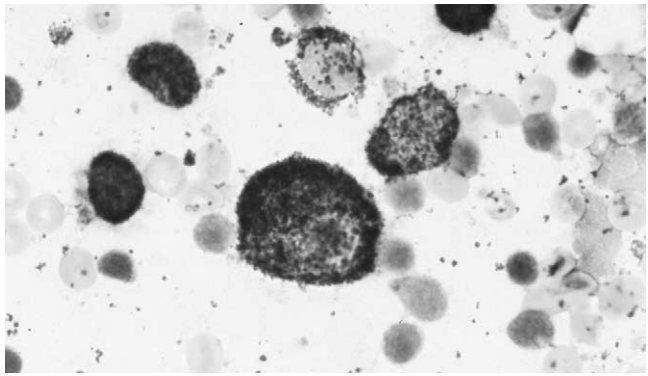

Fig. 17. Higher power view from the same lymph node aspirate shown in Fig. 16. Numerous mast cells are present. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

cells with three or more criteria of malignancy. If moderate to high numbers of spindle cells are observed without appearing malignant, surgical removal of the node and histopathology are suggested for further evaluation.

Myeloproliferative disease may result in the lymph nodes being infiltrated with leukemic cells.

Aspiration of nonlymphoid tissue

Perinodal fat is the most common nonlymphoid tissue accidentally aspirated when attempting a lymph node aspirate. Aspirated fat is recognized

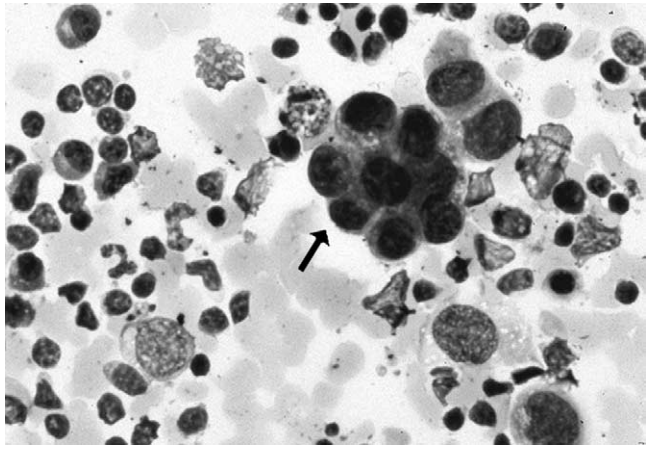

Fig. 18. Lymph node aspirate from a dog with metastatic carcinoma. A cluster of epithelial (carcinoma) cells (*arrow*) is present surrounded by many small lymphocytes and scattered neutrophils and macrophages. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

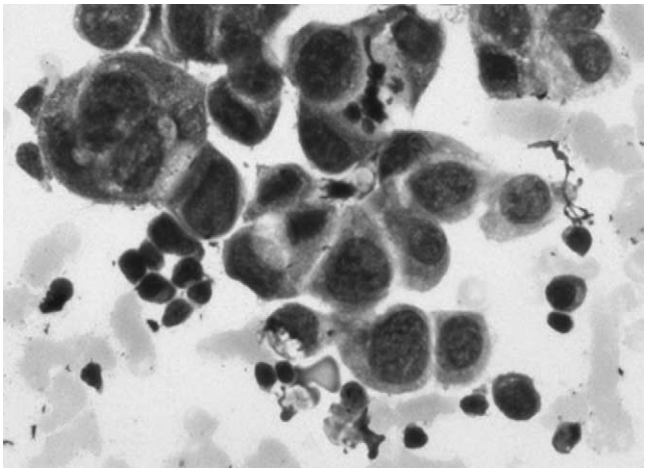

Fig. 19. Higher power view of carcinoma cells from the same lymph node aspirate shown in Fig. 18. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

grossly by its wet (oily) appearance on the smear and its failure to dry. Aspirates from most tissues dry within a few minutes; however, fat appears wet and glistening for days. Microscopically, intact adipocytes appear as large cells with abundant clear cytoplasm and a small nucleus (Fig. 21). They may be present individually or in groups or clusters. Free fat from adipocytes that ruptured during collection or smearing may not be discernible microscopically, because most hematologic stains contain alcohol that dissolves free fat (fat droplets). Occasionally, clear spaces representing the dissolved

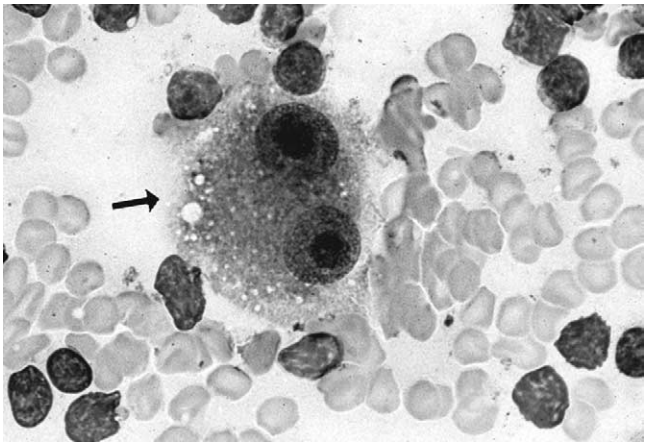

Fig. 20. Lymph node aspirate from a dog with metastatic carcinoma. Large epithelial cells with prominent nucleoli are shown (*arrow*). (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

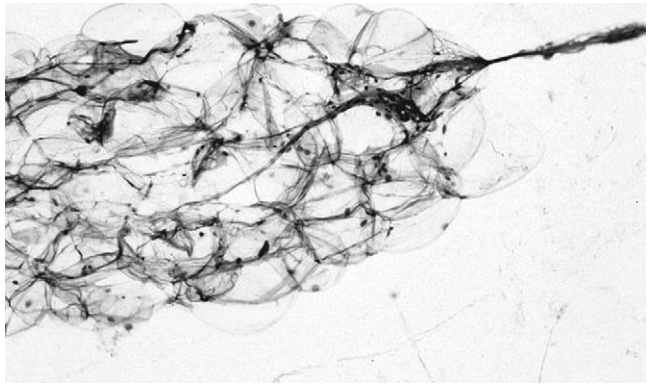

Fig. 21. Aspirate of perinodal fat. Adipocytes are large cells with abundant clear cytoplasm and a small nucleus. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

fat droplets may be observed in the tissue fluid background. Smears that appear fatty should be stained and evaluated, because sufficient lymphoid tissue is often present along with the fat for adequate cytologic evaluation.

The salivary gland is a common tissue accidentally aspirated when attempting to aspirate a submandibular lymph node. Cytologic smears made from salivary gland aspirates typically consist of blood and salivary epithelial cells in a thick eosinophilic mucoprotein background. The salivary epithelial cells are present primarily in clusters, although a few individual cells may be observed (Fig. 22). These cells are uniform in size and shape and have no visible nucleoli. They are medium-sized to large epithelial cells with abundant light blue cytoplasm that may be vacuolated. Their nuclei are

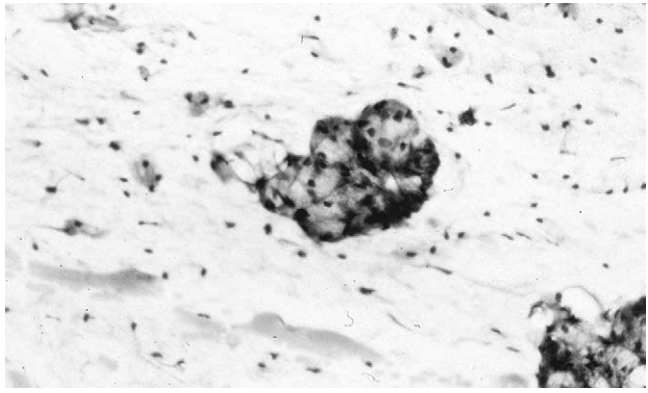

Fig. 22. Aspirate of a submandibular salivary gland. A cluster of normal salivary epithelial cells that are medium sized with abundant light blue vacuolated cytoplasm is shown. These cells are uniform in size and shape with no visible nucleolus. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

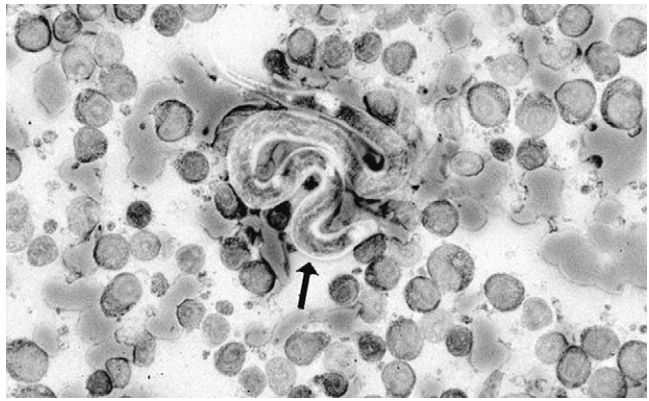

Fig. 23. Lymph node aspirate from a dog with lymphosarcoma showing microfilaria (*arrow*) present secondary to blood contamination. (*Courtesy of* Oklahoma State University, College of Veterinary Medicine, Clinical Pathology Teaching Files, Stillwater, OK.)

roundish and uniform in size and shape with dense chromatin and no visible nucleoli. Location and absence of malignant criteria should help to differentiate normal salivary gland aspirates from metastatic neoplasia in the lymph node.

Miscellaneous

Cornstarch (glove powder) is a common artifact found on cytologic smears and should not be confused with an organism or cell. Cornstarch appears as roundish to imperfectly hexagonal individual granules that stain clear to light blue and have a central refractile zone (fissure).

Microfilaria are occasionally seen on cytologic smears secondary to blood contamination in microfilaremic dogs (Fig. 23). Differentiating *Dirofilaria* larva from *Dipetalonema* larva is difficult to impossible because of shrinkage and other artifacts induced during staining.

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