Diagnostic cytology

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Cytology is not a substitute for histology

but............

GOALS: Diagnostic cytology

- Increase your marketability
- Be able to cover while colleague gone
  - "same" for histopathology coverage
- Diagnose the common lesions
- Know your limitations – save slides for your colleagues review
- Provide clinically useful information
  - Neoplasia -spindle cell tumor......vs.
  - Chronic pyogranulomatous to suppurative regional to locally extensive dermatitis with focal areas of necrosis, collangedelysis and follicular and adnexal atrophy with intralesional organisms
  - DEMODEX + RINGWORM

EASY for YOU

- Know all the diagnoses
- Know the majority of the jargon
- Know about artifacts
- Know about non-diagnostic samples
- When all else fails……………
  recommend histopathology
DIFFICULT for YOU

- DON'T BELIEVE...low confidence
- Histopathology – 1 slide, 5 seconds
- Too many worthless slides
  - non-diagnostic samples
- Learn artifacts, read through them
- Bone marrow – Dr Thrall
- Dotology 101 – organisms
- OIL !!!!! Solution = Throw it out
  - If you need 100X to diagnose neoplasia you need a therapist

Which image do you prefer?

Oil?  High Dry

Which image do you prefer?

Coverslip on top  NO coverslip

Both are High Dry – NO OIL !!

Advantages of cytology

- rapid
- inexpensive
- relatively non-invasive
- establish diagnosis and or treatment plan
- anesthesia not necessary for skin lumps
- basic interpretation can be performed in-clinic
- Recent DVM grads “love” it
  - This is why this discipline will continue to grow and this area of our diagnostic jobs will expand

Cytology vs Histopathology

- Mast cell tumor
- Lymph nodes
- Bone marrow
- Fluids
- Infectious agents
- Vaginal
- Ultrasonography

Gold standard
- Histochemistry
- Immunohistochemistry
- Architecture –
- Grading
- Invasion – B vs M
TODAY

- General principles – inflam vs neoplasia; artifacts
- Skin SQ
- Fluids, e.g. thoracic, abdomen, joint
- Lymph nodes
- Organs
- Bone marrow
- NOT TODAY
  - washes: respiratory, prostate
  - staging of heat in bitches (vaginal cytology)
  - collection, preparation techniques, artifacts
  - more organs, infectious agents, CBC

Your objectives/ Diagnoses

- Septic inflammation
- Non septic inflammation
- Eosinophilic inflammation
- Organisms
  - Crypto/Crypto/blasto/histoblasto/histo
  - Leish/toxo/hyphae
- Hematoma
- Cyst – epidermal
- Sialocele

NEOPLASMS
- Round cell
  - Lymphoma/histiocytoma/plasma cell/TVT/MCT
- Epithelial cell
- Mesenchymal
- Malignant vs. benign

Your objectives/ Diagnoses

- SEPTIC INFLAMMATION
- NON SEPTIC INFLAMMATION
- EOSINOPHILIC INFLAMMATION
- ORGANISMS
  - Crypto/Crypto/blasto/histoblasto/histo
  - Leish/toxo/hyphae
- HEMATOMA
- CYST – EPIDERMAL
- SIALOCELE

NEOPLASMS
- ROUND CELL
  - Lymphoma/histiocytoma/plasma cell/TVT/MCT
- EPITHELIAL CELL
- MESENCHYMAL
- MALIGNANT VS. BENIGN

Basic interpretation

- First find a good area to look at via 4 – 20X objectives
- Do you see neutrophils? #1 nucleated cell?
- Are the cells normal for that location? (not necessary to do for skin lesions)
- If not, is the lesion inflamatory or non-inflamatory? = neutrophils Y or N
- Tumors with inflammation = NEVER try to interpret "naked" nuclei
  - If "100%" naked consider neuroendocrine
    - Carotid body, apocrine gland CA of anal sac

Interpretation skin lesions

- Do neutrophils predominate? Yes then the lesion is inflamatory
- No - then non-inflamatory
  - cyst = or
  - neoplasm = (SCC often have an inflammatory component)

Definitive diagnosis may not be possible (or necessary) on basis of cytology but these general categories are usually sufficient to provide clinically useful information

Inflammation
- Cyst
- Neoplasm
  - Round cell
  - Epithelial
  - Mesenchymal
- Benign vs. malignant
Neutrophils

- HEALTHY NEUTROPHILS
  - nondegenerate
- Nonseptic

Degenerate

Nuclei swell, may fragment, cell loses details, cytoplasm blueish = indirect evidence of sepsis
Or........an old sample...sitting around
Pyknosis, karyolysis, karyorrhexis

Microscopic evaluation

Fluid microscopic evaluation

- Neutrophils often > 90% = active process
- Septic vs. Non-septic
- Indirect vs. Direct Evidence of sepsis
- Degenerate PMNs

Inflammatory lesions

- Neutrophils? Yes – the lesion is inflammatory
- Degenerate cells? = suspect sepsis, bacteria
- Search in PMNs:
  - intracellular = real
  - extracellular = real vs contaminant

ALL bacteria stain blue with Diff Quik........
Except.....
Mycobacterium = clear, colorless; why?
Acid Fast Stain.
Mycobacteria – red-pink, intracellular

Stains for cytology
- Diff Quik - good general purpose stain – USE!
- New methylene blue - good for nuclear detail (e.g. suspect malignancy).
  **BEWARE** if you are not used to this stain you tend to “over interpret”
  and diagnose too many cancers.
- Gram’s stain - seldom necessary
- T blue, iron, immunohistochemistry – only ones I use much are PAS & Dblue
- Can de-stain and re-stain same slide

Staining of smears
- Understained smears - be careful. Diff quik type stains lose their potency with use, not all mast cells are stained and fluids will grow fungi
- Right: Smear stained using Diff Quik, but for insufficient time.
  Note the “ghost” cells in the background. You can re-stain this by dipping 2 more times in the blue (last) fluid
- Above: Same smear dipped a few more times (be careful) in the polychrome (blue) stain. The cells in the background are now clearly visible

Inflammatory lesions
- Use the numbers and types of inflammatory cells to establish a morphologic diagnosis and predict possible etiologies
- Active - >70% neutrophils; abscess will be 100% PMNs
- Pyogranulomatous - mostly neutrophils and with numerous macrophages (monocytes)
- Granulomatous >50% macrophages;
  Lesions consisting mainly of macrophages can resemble neoplasms - KEY be careful

Inflammation
- Neutrophils – degenerate vs. healthy
- Eosinophils – may not be red
- Lymphocytic – liver and fluids RARE in solids
- Granulomatous – don’t dx neoplasia; look for giant cells then search for fungi, yeast, parasite, usual and foreign body.
Cell types encountered

- EOSINOPHILS
- Parasite
- Immune/allergic
- Neoplasms – MCT LSA
- Collagen – cats, bone, eq
- Eotaxin – fibroblasts

Brilliant red granules, right?

- Mucus – tracheal wash
- Serum edema
- Too thick a prep – repeat or ...
- Try thinner areas – move search low mag
- Know what to expect

EOSINOPHILS CAT
- RUST BROWN granules
- Have to recognize eosinophils in tissue before you can suspect correct etiologies

THICK

THINNER AREA OF SLIDE
ROUGH preparation
Fragile cells

Some place on this slide is a “useful – diagnostic” area - SEARCH
Or……….. try ANNTECH or IDEXX anywhere but me

Nuclear debris/strands
Lysed nuclei, nuclei dragged linearly
Don’t misinterpret as fungi, fibrin
Source: rough prep, old sample with cell fragility; septic environment

True fungi – appear as “ghost” outlines; straight lines
Inset = well stained Aspergillus. unusual to see them this clearly

Cell types encountered

- Plasma cells

Macrophages – histiocytes, when “active” have cytoplasmic vacuoles
Fuse and form multinucleated giant cells
Confuse with neoplastic cells!

Inflammatory lesions

Left: Active inflammation – pure population of degenerate neutrophils. Purple droplets in the
backround are droplets of protein and remnants of dead inflammatory cells, not bacteria. Degenerate
neuts = sepsis (vs old sample). LOOK

Right: Chronic granulomatous inflammation – The relatively pure population of macrophages could be misinterpreted as
everalastic cells. Multinucleate

Above: Chronic inflammation – mixed population of neutrophils and large macrophages, one of which
is binucleate
**Blastomycosis**

- 20 X: Find blue blobs/dots at low mag.; extracellular, larger than neutrophils; proceed to higher mag.
- 100 X: Multinucleated giant cell suggests fungal infection. Blue colored yeasts intraacellular.

Usually there is marked inflammation; dog with foot ulcer or respiratory signs.

**Other etiologies…size, location**

- RBC & smaller
- Histoplasma
- Toxoplasma
- Leishmania
- Trypanosomes
- Malassezia

- Neutrophil & bigger
- Cryptococcus
- Blastomycosis
- Rhinosporidiosis
- Coccidiomycosis
- Hyphae
  - Aspergillus
  - Mucor

**Parasites**

**Leishmaniasis**

- Leishmania sp organisms in macrophages lymph node dog.
- Note the small rod-shaped kinetoplast near the nucleus in each organism. Histoplasma organisms are similar in size but do not have kinetoplasts.

**Neoplasia**

- Mass
- #1 nucleated cell is NOT a neutrophil
- "No" neutrophils
  - (SCC has marked inflam)
- Are cells
  - Round individual – round cell tumor
  - Spindle individual – mesenchymal tumor
  - Large, held together – epithelial tumor

**Round cell Epithelial Mesenchymal**

- Cellularity
- High
- High
- Low
- Cells
- Individual
- Clusters
- Individual
- Shape
- Round
- Cubodial
- Spindle

Benign = Uniform vs Malignant = Variable.

- See neutrophils? Are cells individualized or organized? Shape of cells? Shape of nuclei? Variability? Every time answer these?
Round cell Epithelial Mesenchymal

Epithelial
Adenoma vs carcinoma
Sebaceous
Mammary Prostate
Nasal
Transitional
Perianal

Round cell
Lymphoma Plasma cell tumor
MCT TVT
Histiocytoma

Spindle - mesenchymal
-oma vs sarcoma
Fibroma fibrosarcoma
Osteoma osteosarcoma
Hemangioma hemangiosarcoma

Round cell tumor
Purple granules, variable numbers to none

Cytoplasmic granules

MCT – mast cell tumor
Round cell tumor
Purple granules, variable numbers to none

Melanoma - Black, green granules, variable numbers to none
Blurred round/epithelial/spindle cells

Epithelial tumors
- cells in sheets or clusters
- usually many cells present
- distinct cytoplasmic borders + -
- cells often large with abundant cytoplasm
- sometimes show signs of differentiation

Benign – uniform
Malignant – variable

Above. Clusters of epithelial cells from an epithelial tumor. Some of the clusters appear to be forming acini (arrow).
Uniform cells & nuclei = benign

Right. Squamous differentiation of epithelial cells, dog with SCC of the prepuce. Often marked neutrophilic inflam.
Large cells VARIABLE = MALIGNANT

Mast cell tumor - dog

FNA from the lesion on the tip of this 11-y.o. lab is illustrated at right.
One neutrophil, many large round cells with variable numbers of metachromatic granules typical of neoplastic mast cells.
CYTOLOGY provided the diagnosis and treatment plan

Round cell tumors
- cells usually individual: but sometimes are situated closely together and look like they are in small aggregates as in epithelial tumors, don't get confused by this pattern
- usually plenty of cells present
- circular cells with round nuclei, distinct cytoplasmic borders
- cells may be well differentiated, e.g. mast cell tumors

Mast cell tumor dog

In this case the tumor cells are well granulated.
Occasional large mesenchymal cells are also present (arrows).
These are part of the supporting stroma and are not neoplastic.
Aspirate of same lymph node as shown in prior slide, when stained with Wright’s (Giemsa) stain (for blood smears).

Lymphoma

Aspirate from an enlarged lymph node.

1. Nucleated cell is large blast forms. A normal small lymphocyte is indicated by red arrow. Your "ruler" are the rbcs (7u). Mature lymphocytes should be a little larger than rbcs.

2. The small blue droplets in the background are "lymphoglandular bodies" (arrows). These fragments of cytoplasm are common in preparations from hyperplastic or neoplastic lymphoid tissues.

2 y.o. FS dog, 2 cm ulcerated mass at base of left ear. DIAGNOSIS? ...or describe what you see

2 y.o. DIAGNOSIS? or describe what you see

Start with the #1 nucleated, neutrophil? NO, therefore ... tumor

Round nuclei to oval nuclei, fairly uniform, moderate amount of cytoplasm

Round cell tumor = DDx = lymphoma, histiocytoma, TVT, plasma cell

Most likely = histiocytoma based on species, age, location and cytology
2 y.o. FS dog, 2 cm ulcerated mass ear.

Transmissible venereal tumor
Fine needle aspirate from a mass on the penis of a dog
Individual round cells with fairly abundant blue cytoplasm and uniform round nuclei; discrete cytoplasmic vacuoles. Key to the diagnosis is: round cells and...
Location: genitals
The large cell (arrow) with abundant cytoplasm is a non-keratinized squame from the penile or preputial mucosa. NGS

TVTs: round cells, more cytoplasm than in lymphoma, look just like histiocytoma: location location location!!!

Lymphoma – least amt of cytoplasm
TVT, histiocytoma, plasma cell => cytoplasm

PLASMA CELL TUMOR: skin, oral, GI NOT bone = multiple myeloma
CYTOLOGY: round cell tumor, eccentric nuclei, abundant cytoplasm, blue cytoplasm, Golgi apparatus. Look like osteoblasts and vice versa.
Plasma cell tumor: BEHAVIOR- most are benign, malignant forms have variability
giant cells multiple nuclei

We cannot cover the “range” of patterns you will see for each tumor.
EXTRAPOLATE – you know from histopath how more malignant forms
of plasma cell tumors resemble histiocytic tumors.

Round cell tumors
- MCT – granules; Diff Quik; eosinophilis
- Histiocytoma – young dog, >cytoplasm
- TVT – LOCATION, looks like histiocytoma
- Lymphoma – small amt of cytoplasm, blast cells
- Plasma cell – eccentric nuclei, Golgi, abundant cytoplasm
- If in doubt excisional biopsy, at least you RO inflammation, RI neoplasia, round cell, and most of
these are benign = useful information, obtained immediately

Mesenchymal tumors
- exfoliate poorly in FNAs and imprints (except osteosarcomas) - few cells present
- cells typically have elongated nuclei and cytoplasmic tails (spindle cells)
- cells usually individual but sometimes in clusters with intercellular matrix
- active fibroblasts resemble malignant mesenchymal cells – use histopathology

Mesenchymal tumor
No neutrophils
Predominantly fusiform cells = the mass is either a mesenchymal (spindle cell) tumor or granulation tissue.

In general, mesenchymal lesions should be submitted for histopathology as active fibroblasts are difficult to
differentiate from neoplastic fibroblasts and may even have features that suggest malignancy.
Diagnosis: hemangiosarcoma

Cytologic Diagnosis?
Mesenchymal cell tumor (possibly granulation tissue) is there a MASS? If so, cancer more likely.

Hx. – 10cm. Diameter non-ulcerated mass left hind leg above stif. Neoplasia much more likely than granulation tissue.
Hemangiopericytoma

- Common tumor of dogs, legs, body

Hemangiopericytoma – grading schemes based on histopathology. Low grade recurrence rate of 25% after surgical excision, survival time of 118 weeks, and 2% metastatic rate. High-grade sarcomas – recurrence rate of 62% after surgical excision, mean survival time of 49 weeks and metastatic rate of 15%.

Spindle cell neoplasia

Don't worry about the exact name!! The grading schemes DO NOT differentiate based on the name: fibrosarcoma, hemangiopericytoma, neurofibrosarcoma, peripheral nerve sheath tumor, poorly differentiated sarcoma etc. Use this to your advantage on cytologic specimens.

Grading schemes are based on histopathology, the mitotic index (some use other criteria). So the following comment is for ALL the tumors listed above.

Low grade canine cutaneous sarcomas (less than 9 mitotic figures per 10,400x fields) have a recurrence rate of 25% after surgical excision, a median survival time of 118 weeks, and a 2% metastatic rate. High-grade sarcomas have a recurrence rate of 62% after surgical excision, mean survival time of 49 weeks and a metastatic rate of 15%.

Spindle cell neoplasia

Don't worry about the exact name!! Differentiate neoplasia vs. granulation tissue. So how will you solve this?

Hx. Prior excision? Age of animal
PEx. Mass? Ulcer? Flat vs. raised, location
Cytology. Inflammation also present vs no concurrent inflammation, overall cellularity = >#cells>likelihood cancer.
THINK

ODDS = dog – hemangiopericytoma cat – fibrosarcoma
horse – granulation tissue vs sarcoid

Mass in the ventral neck region of an adult dog – what is your diagnosis?

The aspirate at right shows ___________________. You fill in the blank.

Diagnosis?
Plan?

Melanoma

The aspirate shows some large cells with multiple, green/black intracytoplasmic granules. Similar granules from ruptured cells are scattered throughout the background. The naked nuclei are from the ruptured tumor cells.
Histochemical stains
Immunohistochemical stains

Intramedullary pin
Mass
Bone lysis...where is the femur?
DDx.
Osteomyelitis
Osteosarcoma
Other cancer
Plan – aspirate, cytology and culture.

Cat ... thoughts?
This is not osteomyelitis, no neutrophils
Culture not needed
Osteosarcoma most likely
Amputation? Chemotherapy?
PLAN?

Cytol left Histopath. Right – Diagnosis?
See neutrophils? Are cells individualized or organized? Shape of cells? Shape of nuclei? Variability? Every time answer these?

Diagnosis: Osteosarcoma

Key to the diagnosis: LOCATION = bone with lysis, morphology = spindle shapes, product, note the pink material in both preparations, this is osteoid which obviously helps with the diagnosis.

Fine needle aspirate from the lytic lesion (below right) in the radius of a dog — what is your diagnosis?

Osteosarcoma

Malignant osteoblasts have features of normal reactive osteoblasts (eccentric nuclei, basophilic cytoplasm, prominent Golgi apparatus) but usually show convincing features of malignancy. Highly reactive osteoblasts (e.g. at recent fracture sites) may be difficult to distinguish from malignant osteoblasts – histology on aspirated cases.
Lytic bone lesion

Osteosarcoma vs. Multiple myeloma

How do you differentiate?...know characteristics of these tumors and apply this information to case.

OSA
- Lame, thin, sick
- One bone one lesion
- Characteristic breed
- Characteristic location
- Radiographic pattern
- Osteolysis + osteoproduction
- Normocalcemia & protein
- Osteoid; variability, giant cells
- Anaplastic features, flag cells

MULTIPLE MYELOMA
- Lame, thin, sick
- Multiple bones multiple holes
- Any breed
- Any bone
- Multiple foci osteolysis
- Discrete holes
- 10% hypercalcemic; monoclonal
- Round cells, Golgi, some are
- Very well differentiated

CytoLOGY

OSA
- Spindle cells
- Greater variability
- Multinucleated cells
- Matrix
- No bone marrow elements
- Osteolysis + osteoproduction
- Osteoid; variability, giant cells
- Anaplastic features, flag cells

MULTIPLE MYELOMA
- Round cells
- More uniformity
- Binucleate cells
- Mott cells
- Bone marrow still present
- Discrete holes
- Round cells, Golgi, some are
- Very well differentiated

Lipoma vs “missed” lymph node/tissue

Lonicera algis - MISS

General features of malignancy

- Hypercellularity of smears
- Pleomorphism of cells within same cell line - variable size, shape, nucleus:cytoplasmic ratio
- Disorganisation of cells within clusters
- Occasional very large cells, large nuclei and nucleoli
- Variability
- Epithelial mesenchymal round cells
Nuclear criteria of malignancy
these are better than cellular features

- increased nuclear size
- variation in nuclear size
- large, irregular-shaped nucleoli
- coarse chromatin pattern
- multinucleation (especially if variable size)
- increased mitotic figures

At least 3 nuclear criteria of malignancy should be present for a confident diagnosis of malignancy unless you know the biologic behavior of the tumor in question e.g. if it is an oral melanoma you don’t need any of the above.

Benign tumors
these are epithelial cells: organized, adhered

Characteristics of malignancy

Fine needle aspirate from the lung of a dog with histiocytic sarcoma
Note the huge binucleate cell with massive nuclei and multiple, irregular shaped nucleoli
The erythrocytes and neutrophils in the field provide an indication of the size of the tumor cell

Thoracic fluid
Note clusters / acini in lower photo and the variability in size and shapes of "everything", the clusters, cells and nuclei
DON’T ever diagnose cancer on ONE cell but the adjacent one is pretty good. Compare size of nucleus to the neutrophils

Characteristics of malignancy

Cluster of cells with large nuclei, variable nuclear size, coarse nuclear chromatin pattern and a high but variable N:C ratio. The large size of the tumor cells can be appreciated when they are compared with an RBC (arrow).

6 y.o. cat, note mass at base of neck (arrow). Representative aspirates in these two images, diagnosis?
Injection site sarcoma, fibrosarcoma with giant cells, giant cell tumor of soft parts. Histo/cytol comparison.

Some contain "foreign" material.

Diagnosis?

Circumanal adenoma = perianal adenoma NOT anal sac adenocarcinoma

"Hepatoid" cells

Anal sac apocrine gland adenocarcinoma: females, hypercalcemic, MALIGNANT

Large arrow – tumor, despite small size it had already advanced into the pelvic inlet = metastasis.

Small arrow – indicates the brown rim of apocrine glands that secrete into the anal sacs and that give rise to this tumor.

Anal sac apocrine gland adenocarcinoma – cytology left; histology to right. Tumor cells look benign to me but they are from an abdominal metastasis. Knowing the biologic behavior of certain tumors is a better predictor of malignancy than looking at the cytology or histology. These tumors tend to produce naked nuclei.
What do you see? What do you observe first?

See neutrophils? Are cells individualized or organized? Shape of cells? Shape of nuclei? Variability? Every time answer these questions.

Transitional cell carcinoma

Note how well cytology and histology resemble each other. Diagnosis on cytology is epithelial tumor, malignant, TCC. Diagnosis on histopathology is TCC metastatic to regional lymph node. Mets were also in the lungs. 20% of the cases of TCC have detectable pulmonary mets at time of first diagnosis.

Adenocarcinoma

Cytology on conc. fluid prep is to left; a cell pellet was prepared of the fluid and histopathology of the pellet is on the right.

Non-inflammatory lesions

- neoplasia, cysts, hematoma
- hyperplasia if an organ, not practical for skin or SQ

Epidermal inclusion cyst

The stratified squamous epithelium and keratinized squames in the histologic prep are reflected in the adjacent cytologic preparations. Rectangular cholesterol crystals are often present (arrow), and most likely develop through crystallization of cholesterol from the membranes of dead cells.

Epidermal inclusion cyst

The sample may look like "debris" or a vaginal preparation because of the keratinized squames and amorphous cellular debris. Rectangular cholesterol crystals are often present (arrow).
Hematoma Hemorrhage

Varying amounts of blood

Soft fluctuant swelling, ear, SQ
Aspirate – gross, direct slide prep
Gross – Red = hematoma vs blood contamination
Slide – look for platelets = blood contamination
erythrophagocytosis = hematoma
 hemosiderin = hematoma

Presence of platelets indicates blood contamination, rather than hematoma (or hemoabdomen), in which one does NOT see platelets

Hemangiosarcoma

Hematoma

40 X
Mixed inflam
Note cytophagia

Erythrophagocytosis hemosiderin pigment

SC mass, dog

Splenic mass
Comment I use in cytologic and histologic reports

MAT – what would you like/recommend?

If acanthocytes, nucleated red blood cells and/or fragmented red blood cells are present in CBC I would be suspicious there is an underlying hemangiosarcoma

Sialocoele
Saliva leaks stimulating inflammation
- Dogs
- Swelling angle of mandible
- DDx.: sialocoele, hematoma, lymphoma, salivary tumor, carotid body tumor

Plan – aspirational cytology

Few large mononuclear cells, no PMNs
Rowing of RBCS – thick viscous fluid (joints)

Sialocoele
Hematoidin crystal = rbc break down pigment, indicates prior hemorrhage
Large finely vacuolated cells = salivary cells
Single PMN, there were more in adjacent fields

Artifacts and contaminants
- Squames
- Glove powder
- Stain precipitate
- Ultrasound gel (magenta colored material)
Talc crystals

circular, core dot, retractile, groups

Conventional and polarized microscopy

Other etiologies...size, location

- RBC & smaller
- Histoplasma
- Toxoplasma
- Leishmania
- Trypanosomes
- Malassezia
- Neutrophil & bigger
- Cryptococcus
- Blastomyces
- Rhinosporidiosis
- Coccidioidomycosis
- Hyphae
  - Aspergillus
  - Mucor
- Parasites

Inflammatory lesions

This cat has a swelling over the bridge of its nose. Fine needle aspirates reveal a mixed population of inflammatory cells, predominantly neutrophils and macrophages. Many of the macrophages contain variable numbers of small oval organisms with a thick, unstained capsule. Some organisms are also free in the background. These organisms are typical of Cryptococcus neoformans.
**Blastomycosis**

- 20 X: Find blue blobs/dots at low magnification, extracellular, larger than neutrophils; proceed to higher magnification.
- 100 X: Multinucleated giant cell suggests fungal infection. Blue-colored yeasts intracellular.

Usually there is marked inflammation; dog with foot ulcer or respiratory signs.

**Blastomycosis**

- Dog, 6 y.o., foot ulcer, labored breathing. Thoracic radiograph = interstitial pneumonia. Aspiration of foot lesion or TTW.

**Fungal Mycotic - hyphae**

- Location of disease: Nasal - mass or osteolysis, Bone, Lung, Stomach - GI, Eye - horse.

**Fungal Mycotic - hyphae**

**Nasal aspergillosis - dog**

The tiny, blue-green refractile structures (arrows) in this nasal flush from a dog are spores derived from the fruiting bodies of *Aspergillus sp.* Hyphal forms are seldom seen in nasal flushes. Several neutrophils and erythrocytes are also present and there is a considerable amount of smeared nuclear material.

**Lungworm - cat**

Lungworm larva in a trans-tracheal wash from a coughing kitten. The cells in the background are predominantly macrophages, some of which contain granular pigment, probably hemosiderin. Plasma cells and eosinophils are also present.
**Histoplasmosis - cat**

*Histoplasma capsulatum* in a macrophage from a cat – numerous small organisms, intracellular.

Ruptured macrophage releasing *Histoplasma capsulatum* organisms, with an eccentric nucleus and surrounded by a halo. Two intact macrophages containing organisms are also present.

**Leishmaniasis**

*Leishmania* sp organisms in macrophages from a lymph node of a dog.

Note the small rod-shaped kinetoplast near the nucleus in each organism. *Histoplasma* organisms are similar in size but do not have kinetoplasts.

**Large numbers of Leishmania sp** in an aspirate of an enlarged lymph node of a cat. Animal may have skin lesions, enlarged lymph node, joint, bone marrow, organ lesions.

The organisms are either in macrophages or free in the background. Note the plasma cell near the center of the field (arrow).

Leishmania are in large numbers, easy to find, they have 2 DOTS!

**Toxoplasmosis - cat**

*Toxoplasma gondii* organisms in macrophages (above) and free tachyzoites (right) in a tracheobronchial wash from a cat.

Elongated; banana shaped

Low numbers, hard to find

**Infectious conjunctivitis - cat**

Smear prepared from a conjunctival swab from a cat with conjunctivitis.

The large cells with features of non-keratinized squames are conjunctival epithelial cells. Several of them have multiple fine, purple bodies consistent with *Mycoplasma felis* on their surface.

A couple of cells also have 2 or 3 blue-staining intracellular structures with a finely-granular appearance (arrows). These are most likely elementary bodies of *Chlamydia sp*.

Also note the neutrophils, indicating acute inflammation.

**Otitis externa – dog**

Large numbers of *Malassezia pachydermatis* in a smear prepared from an ear swab of a pup with otitis externa. The large angular structure is a keratinized squame.

These small budding yeasts with a typical footprint appearance are found in small numbers in ear swabs from many clinically normal dogs and cats, but when present in large numbers (>10 per high power field) they are likely to be significant.

*Malassezia pachydermatis* can also be involved in some exudative skin conditions of dogs, either as a primary or secondary agent.
Otitis externa – dog

In this case the smear contains large numbers of rod-shaped bacteria, in addition to degenerate neutrophils.

*Pseudomonas aeruginosa* was cultured from the ear.

Examination of ear swabs should be routine in dogs and cats with otitis externa to ensure that the appropriate therapy is chosen.