



**Unraveling the
Mystery of Melanoma**

Wendy Blount, DVM



BOLAND VET SALES
SAMSUNG



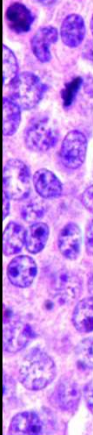
JORGENSEN
LABORATORIES



covetrus

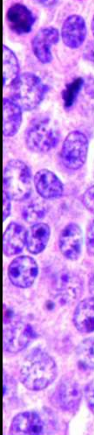


Practical
Vet & Med
SERVICES



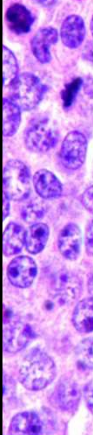
Canine Melanoma

- 4% of all canine tumors
- Most common oral tumor in the dog
- Like MCT, relatively unpredictable tumors
 - Spontaneous regression of metastasis is more likely with this tumor compared to others
 - Benign histopath is sometimes followed by malignant behavior
 - Malignant histopath is sometimes followed by benign behavior
 - Studies are not always repeatable



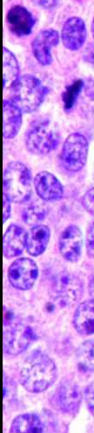
Oral Tumors in Dogs

- Malignant melanoma most likely
- Others:
 - Squamous cell carcinoma
 - fibrosarcomas
 - Epulides and other odontogenic tumors
 - Plasma cell tumor
 - Alone or part of multiple myeloma



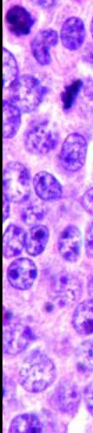
Diagnosis - Cytology

- Melanocytes can be identified on cytology if granulated
- Spindle, round or epithelioid cells
- Must be distinguished from “melanophages” occurring with dermatopilic lymphoid hyperplasia in dark skinned dogs
 - Macrophages that have taken up melanin



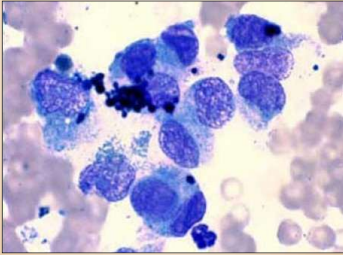
Diagnosis - Cytology

- Melanin granules
 - Range from clear to golden to dark brown-green-black
 - Fine, coarse or needle-like
 - Can be intracellular and/or extracellular
- Tumors containing clear melanosomes are the most malignant and called “amelanotic melanoma”
 - May require immunohistochemistry to differentiate from anaplastic sarcoma

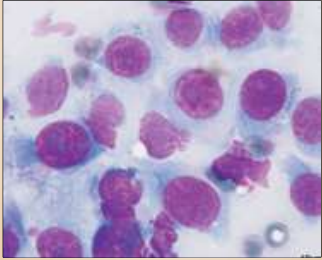


Diagnosis - Cytology

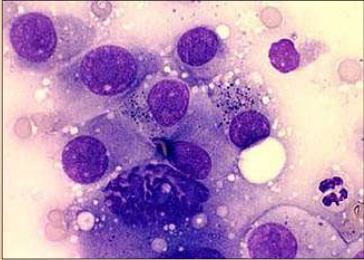
Mass Cytologies



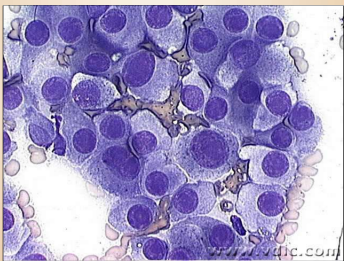
Diagnosis - Cytology
Mass Cytologies



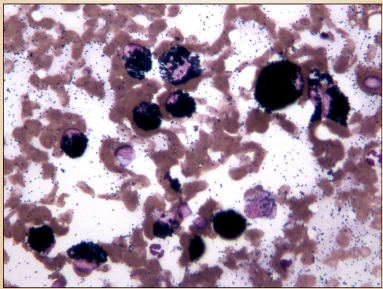
Diagnosis - Cytology
Mass Cytologies




Diagnosis - Cytology
Mass Cytologies




Diagnosis - Cytology
Mass Cytologies

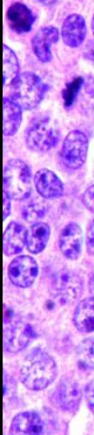


Diagnosis - Cytology
Mass Cytologies



Mom's Third 25th Birthday - Adventures

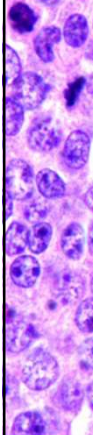




Mom's Third 25th Birthday - Adventures

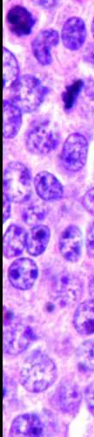
If one advances confidently in the direction of his dreams, and endeavors to live the life which he has imagined, he will meet with a success unexpected in common hours.
--Henry David Thoreau

Greatness, after all, in spite of its name, appears to be not so much a certain size as a certain quality in human lives. It may be present in lives whose range is very small.
--Phillips Brooks



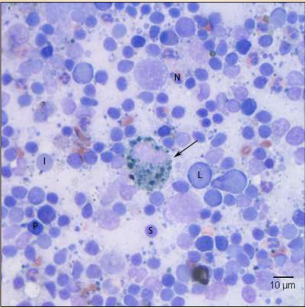
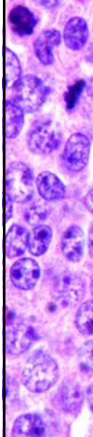
Diagnosis - Cytology

- Lymph node aspirates
 - Mesenchymal cells containing melanin granules in clusters = metastasis
 - Macrophages seen singly containing melanin = dermatophilic lymph node hyperplasia
 - Mesenchymal cells filling the node = metastasis



Diagnosis - Cytology

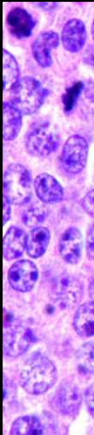
Lymph Node Cytologies

Staging

Why stage melanomas?

- Prognosis for melanoma is extremely variable
 - tumor stage is a prognosticating variable
- Why take a biopsy if cytology is diagnostic?
 - Histopathologic parameters affect prognosis
 - Dirty borders indicate more surgery if possible
- most important for the most malignant
 - Cats with iris masses
 - Dogs with masses on digits and in the mouth

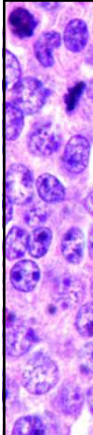


Staging – Oral Melanomas

- **Stage I** – <2cm tumor diameter
- **Stage II** - 2-4cm tumor diameter
- **Stage III** - ≥4cm tumor diameter
 - And/or lymph node metastasis
- **Stage IV** – distant metastasis

Is a 2 cm tumor the same in a Rottweiler and a chihuahua?

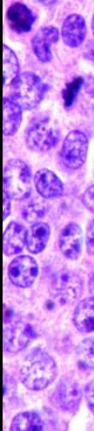
- Patient size has not been considered with respect to tumor size and staging



Staging – Digital Melanomas

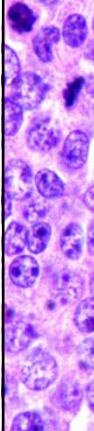
- **Stage I** – <2cm tumor and superficial
- **Stage II** - 2-5cm tumor, minimal invasion
- **Stage III** - ≥5cm tumor diameter
 - And/or subcutis invasion
- **Stage IV** – invading fascia or bone

- Metastasis free interval inversely associated with tumor stage



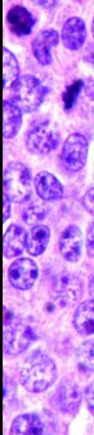
Staging

- CBC, Profile, UA
- 3 view chest films (RadBLUE®)
- local lymph node aspiration and cytology
 - ipsilateral and contralateral nodes for oral melanoma due to variability in draining patterns
 - whether lymphadenomegaly is present or not
 - 70% of enlarged lymph nodes contain metastasis
 - 40% of normal sized lymph nodes contain metastasis
- abdominal ultrasound especially if “hot” location – mucocutaneous junction
 - oral cavity & mucosal surface of the lips
 - Feet – foot pad, nail bed
 - US abdominal lymph nodes, liver, adrenal glands



Treatment

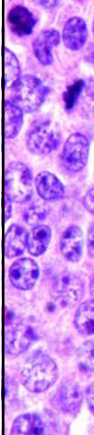
- Surgery
 - mainstay for melanomas on haired skin
 - Typically behave benignly
 - Oral and digital melanomas typically behave malignantly (oral even more so)
 - Oral melanosarcomas may or may not be resectable (especially maxillary)
 - Lip melanomas can go either way
 - IHC Ki67 can help ([MSU](#))
 - Toes usually amputated for histopath
- **Chemo is often ineffective**
- Radiation - melanomas respond well



Treatment

Palliative Therapy

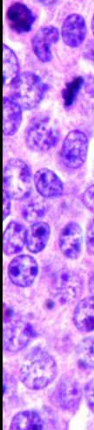
- Piroxicam
 - inhibition of cyclooxygenase 2 (COX-2) expressed on carcinoma cells
 - cyclo-oxygenases lead to the formation of prostaglandins
 - Prostaglandins (E2 series) inhibit natural killer (NK) cell function
 - NK cells recognize tumor associated cell surface antigens and may mediate cell death
 - Inhibition of tumor angiogenesis



Treatment

Palliative Therapy

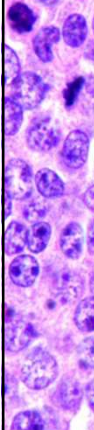
- Piroxicam
 - Unlikely to shrink the tumor significantly
 - Likely will palliate tumor associated pain and inflammation
 - May slow progression of disease
 - Other COX2 inhibitors might be equally effective with fewer side effects
 - GI bleeding, nephrotoxicity
 - 0.3 mg/kg PO SID to QOD
 - Monitor BUN/creat




Treatment

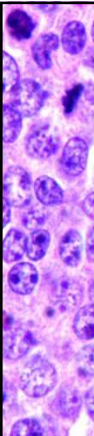
Palliative Therapy

- Cimetidine ([Grungy](#))
 - Supportive studies in horses
 - promote apoptosis in some cancers
 - inhibit angiogenesis
 - enhance the host immune response against tumor cells by blocking T-cell suppression
 - Block cell growth-promoting activity of histamine in colon cancer and melanoma cell lines
 - Might be used to promote stable disease or treat small amounts of microscopic disease, and would NOT expect to decrease the size of gross disease
 - COX2 inhibitor better choice for antiangiogenesis



Mom's Third 25th Birthday - Hospitality

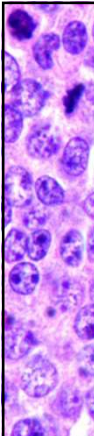




Mom's Third 25th Birthday - Hospitality

"Could a greater miracle take place than to look through each others' eyes for an instant?"
--Henry Thoreau

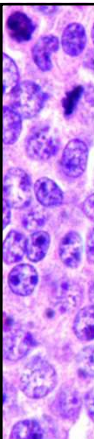
"Don't expect to build up the weak by pulling down the strong."
-- Calvin Coolidge



Treatment – Oral Melanomas

Surgery

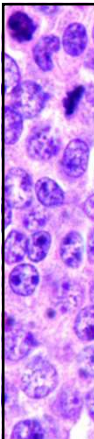
- Maxillectomy and mandibulectomy carry inherent morbidity
- Client satisfaction with this procedure is 85-90%
- Complete staging is indicated with larger resections
 - Distant metastasis would preclude large resection, as survival is likely months



Treatment – Oral Melanomas

Radiation therapy

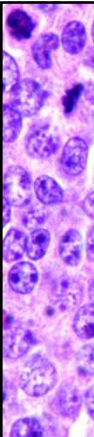
- effective for local control
- Indicated when:
 - Tumor not resectable
 - Couldn't get clean borders on resection
 - Lymph node but not distant metastasis
- Coarse fractionation better than fine
 - Larger less frequent doses
 - Once a week to every other week




Treatment – Oral Melanomas

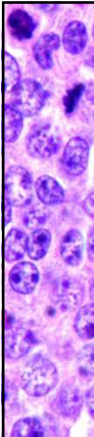
Is chemo helpful after surgery?

- Not really
- Most studies show that chemo plays an insignificant role in management of canine melanoma
- 20% overall response rate
- Does not affect survival time



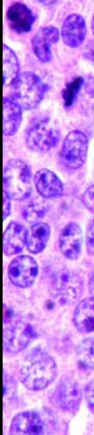
Treatment – Melanoma Vaccine

- Targets the tyrosinase family
- Tyrosinase is a glycoprotein in the melanosome essential to melanin synthesis
- Immunization induces antibodies and cytotoxic T-cells against melanoma
- Conditionally licensed in 2007 and fully licensed in 2009
- Oncept 



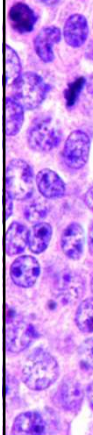
Treatment – Melanoma Vaccine

- Appropriate when there is minimal residual disease after surgery
- **immune training is believed to take months for full effectiveness**
- most dogs with gross disease or mets simply don't live long enough to see the results
- As with most chemo, the larger tumor burden, the lower likelihood for a successful response
- In most cases, must get it through an oncologist



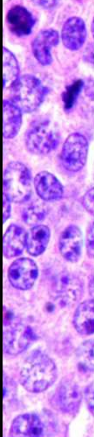
Treatment – Melanoma Vaccine

- Initial study on digital melanoma showed improved MST when added to surgery
- Recent studies question efficacy
- Two show no improvement in survival time when vaccine is added to surgery or radiation
- One study shows shorter MST when the vaccine is added
- Remember... studies are not always repeatable with melanoma



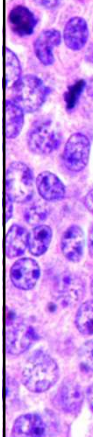
Treatment – Melanoma Vaccine

- Digital melanoma (Manley et al, JVIM 2011)
 - improved survival compared to digit amputation only
 - decreased prognosis for dogs with advanced stage disease
 - Decreased prognosis with increased time from amputation to start of vaccination



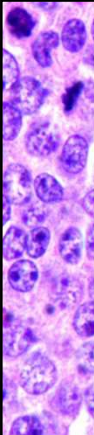
Treatment – Melanoma Vaccine

- \$500 per dose – COST
- 1 injection every 2 weeks for 4 treatments
- Then every 6 months for 2 years
- Total drug cost \$4,000
- Usually sold 4 doses (\$2,000) at a time
- Has a special injector that diffuses the injection for better immune response (BioJect)



Prognosis

- Extremely variable
- Depends on:
 - Anatomic site
 - Tumor size
 - Stage
 - Histology



Prognosis – Digital Melanomas

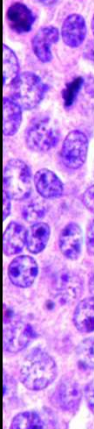
- Amputation with no metastasis to lymph node or elsewhere
 - Median survival 12 months
- 30-40% have detectable metastasis at presentation
- Most have undetected metastasis at presentation (70-75%)



Mom's Third 25th Birthday

Create... Improvise... Think Big!!

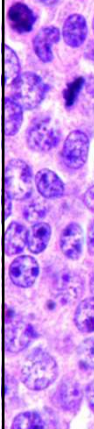




Mom's Third 25th Birthday
Create... Improvise... Think Big!!

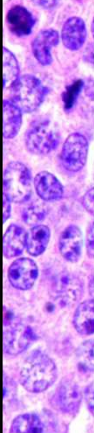
"I can't change the direction of the wind, but I can adjust my sails to always reach my destination."
-- Jimmy Dean

Every time man makes a new experiment, he always learns more. He cannot learn less.
--R. Buckminster Fuller



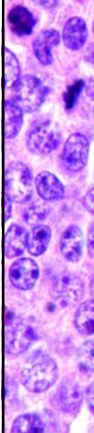
Prognosis – Digital Melanomas

- Surgery only
 - 50% alive at one year
 - 11-13% alive at 2 years
- Surgery plus vaccine, no mets at Sx
 - Stage I – 93% alive at 3 yrs
 - Stage II – 79% alive at 1 yr, 64% alive at 2 yrs
 - Stage III – 77% alive at 1 yr, 65% alive at 2 yrs, 57% alive at 3 yrs
 - Stage IV – 40% alive at 1 yr, 19% alive at 2 yrs



Prognosis – Oral Melanomas

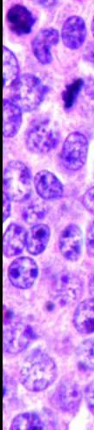
- Factors affecting prognosis
 - tumor size (**2-4 cm**)
 - Incomplete surgical margins is worse
 - Location – caudal mandibular, rostral maxillary are worse
 - **Mitotic index > 3/10HPF** is worse
 - Bony invasion (osteolysis) is worse



Prognosis – Oral Melanomas

- Phil Bergman reports clinical experience
 - A handful of cases each year with benign histopath and malignant behavior
- Bostock et al (Vet Pathol 2001)
 - 3/7 dogs with benign histopathology die of malignant melanoma

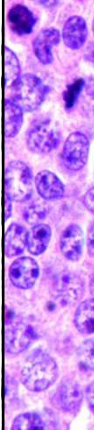
histopathology might not always predict tumor behavior well



Prognosis – Oral Melanomas

- With surgery only (MacEwen et al)
 - Stage I (<2 cm) – MST 17-18 months
 - Stage II (2-4 cm) – 5-6 months (Vx 1 year)
 - Stage III (>4 cm) – 3 months (Vx 1 year)
- Surgery plus radiation and/or chemo
 - Stage I – 12-15 months
 - Dogs die of metastasis, not local recurrence
 - Sx not usually recommended for stage IV

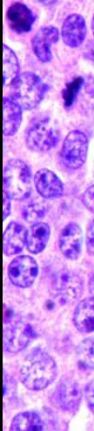
Radiation and chemo do not prevent metastasis



Prognosis – Oral Melanomas

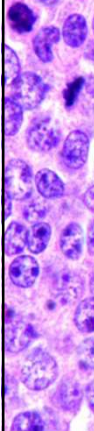
radiation treatments when unresectable

- 50-70% complete remission
- 25-30% partial remission
- Up to 25% do not respond
- **Can increase quality of life significantly by removing or palliating the oral lesion**
- **May not increase survival time**



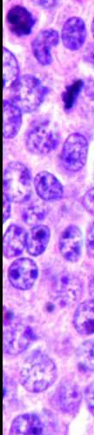
Prognosis – Melanomas on Haired Skin

- Melanomas on haired skin NOT proximal to mucosal margins or toes behave benignly
 - **Surgery is usually curative**
 - Histopath is recommended, but less predictive compared to other tumors
 - Imperative for evaluation of surgical borders
- Prognostic immunohistopathology is available at AMC and MSU
 - AMC - Flaherty Comparative Oncology Laboratory (212-329-8675)
 - [MSU Brochure](#) - [MSU Form](#)



Prognosis – Melanomas on Haired Skin

- Malignant haired skin melanomas are rare but possible
 - 45% of dogs with malignant skin tumors die of their disease within 1 year
- Melanoma histopath is prone to inaccuracy
 - **8% of dogs with skin melanomas of benign histopath with clean borders die of melanoma**
- **Mitotic index** is important
 - <10% of dogs with haired-skin melanoma of mitotic index ≤ 2 died from their tumor within 2 years
 - >70% of dogs with mitotic index ≥ 3 die within 2 years



Prognosis – Melanomas on Haired Skin

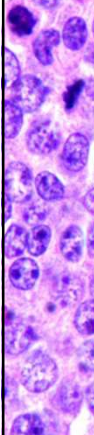
Take Home Points

Malignant haired skin melanomas are the exception rather than the rule

- But when they are malignant, they behave very poorly
- **Cutaneous melanomas should be removed**

Stage I skin melanoma (<2cm) with benign histopath and clean borders does not get a clean bill of health

- 1 out of 12-13 (8%) die of melanoma
- The rest are cured

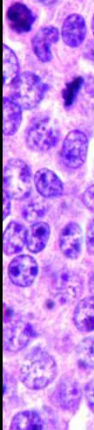


Prognosis – Melanomas on Haired Skin


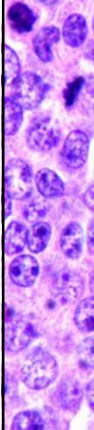
Indications that a melanoma has been removed – SEND FOR HISTOPATH

- Cytology – do a scraping after removal, before you put the mass in formalin
- Pigmentation of the tumor (**Pocket**)

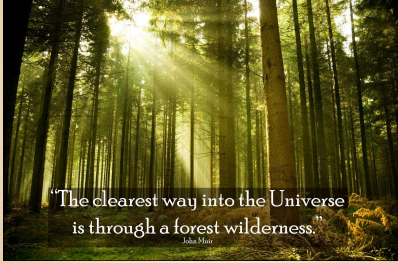
[Client Handout on Melanoma](#)



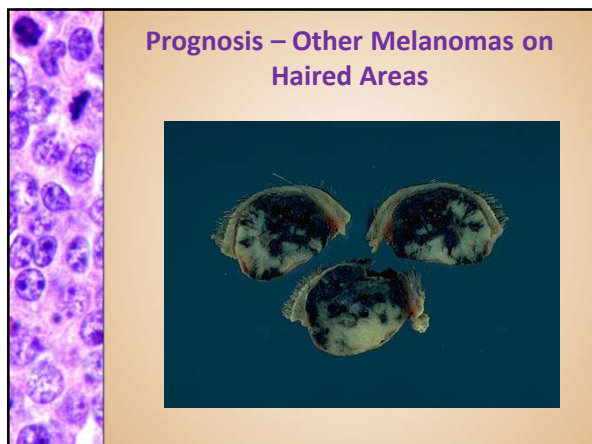
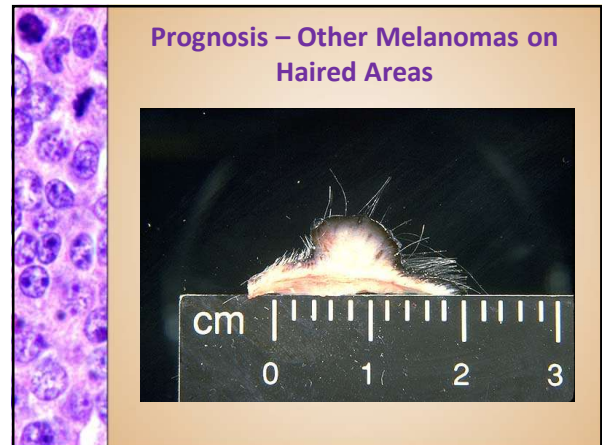
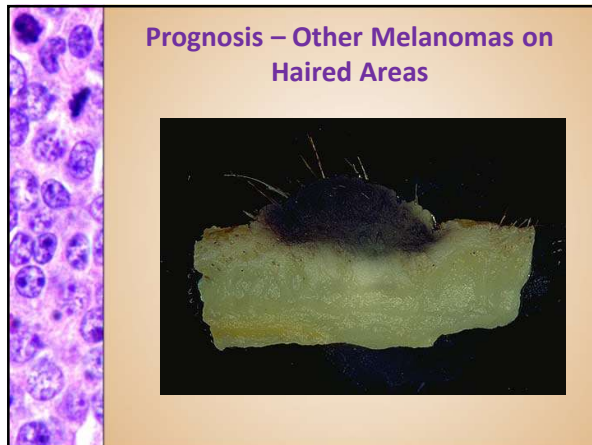
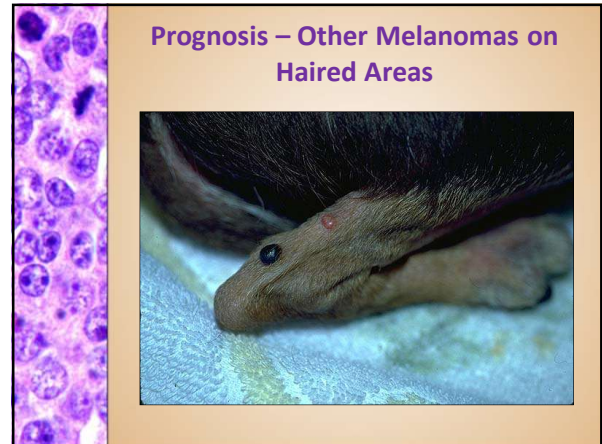
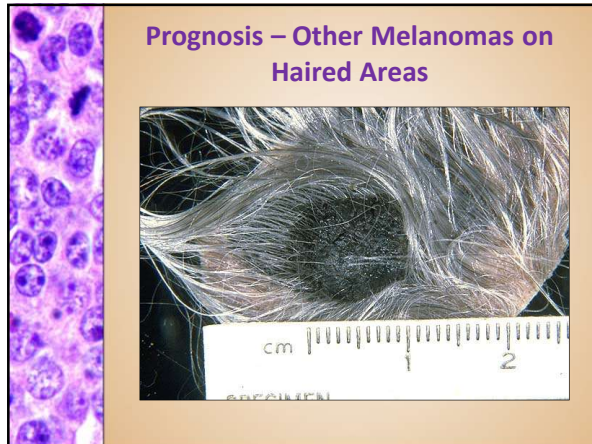
Prognosis – Melanomas on Haired Skin

Mom's Third 25th Birthday - Wilderness

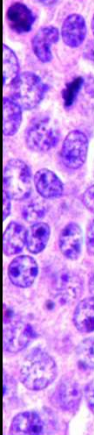


"The clearest way into the Universe is through a forest wilderness."
John Muir



Ocular Melanoma

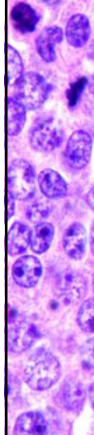
- Usually arise in the anterior chamber
- Rarely arise from the eyelid, orbit, conjunctiva, or posterior uvea
- Behavior is different from the melanomas of melanocyte origin
 - Ocular melanomas are of neuroectodermal origin rather than mesenchymal origin as in the rest of the body



Ocular Melanoma

Cats

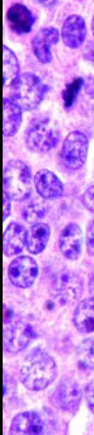
- Significant risk of metastatic disease and tumor related mortality
 - Mortality 30-50% when neglected
- Diffuse transformation of melanocytes on the anterior iris surface
 - CC – “one eye changed color”
 - CC – “pupil is always dilated”
- Prolonged pre-malignant phase
 - Look like iris freckles and nevi
 - Metastasis can take 2-3 years to develop



Ocular Melanoma

Cats

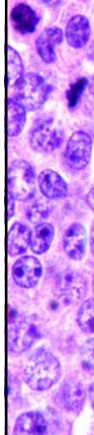
- Distinguishing nevi from malignancy
 - **Nevi are static or slowly evolving** single or multiple pigmented lesions
 - Can appear elevated and slowly enlarge
 - Can appear as bilateral concentric rings of pigmentation (target eyes)
 - **Malignancies progress over time**
 - Diffuse or coalescing multifocal proliferation
 - Cells exfoliate into the anterior chamber and can cause **glaucoma**
 - **Tumor emboli in scleral vessels – grave prognosis**



Ocular Melanoma

Cats

- **Recheck dark spots on the iris every 2-3 months**
- Significant progression since the last visit indicates removal of the eye
- Glaucoma indicates the same
- *Iridectomy* or *laser ablation* reserved for slowly growing isolated pigmented iridal lesions which are likely benign



Ocular Melanoma

Cats


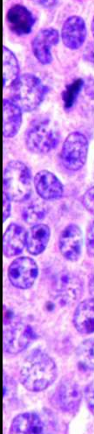



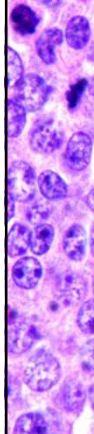
Photo courtesy of Dr. Ian Northing ©2009



Mom's Third 25th Birthday - Joy



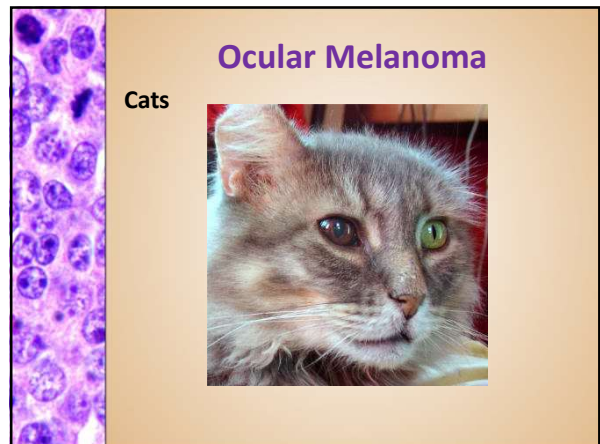
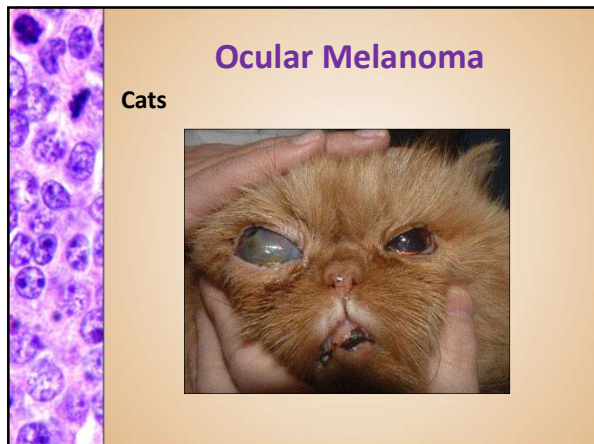
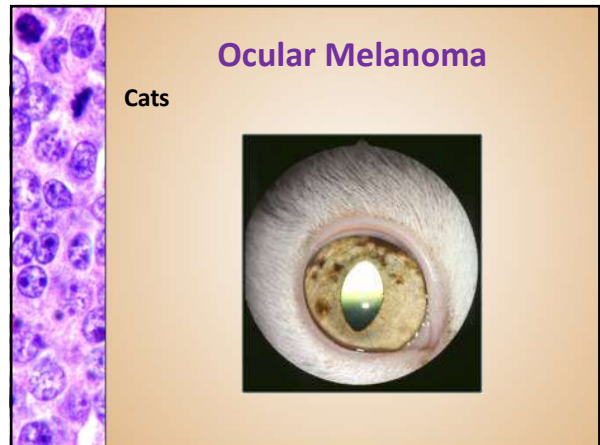
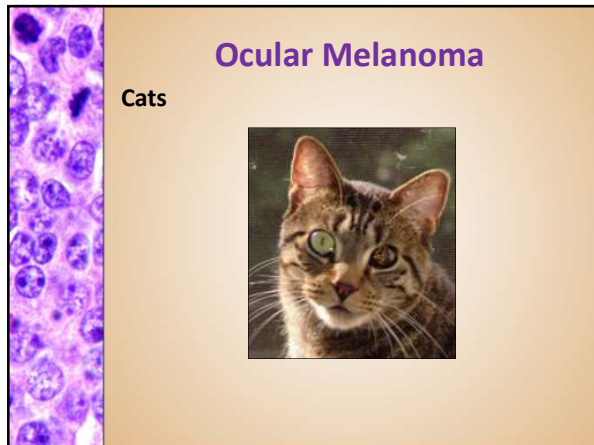
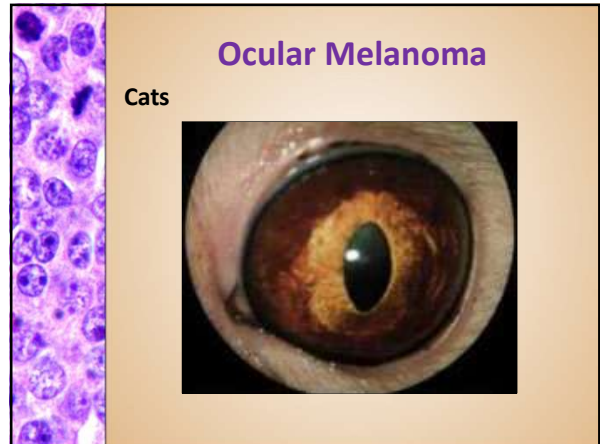
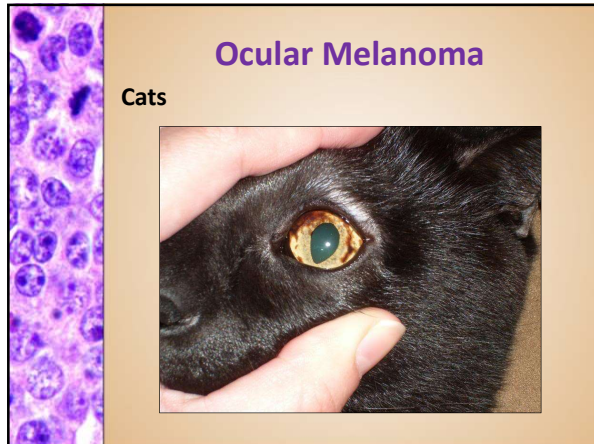
EMERSON

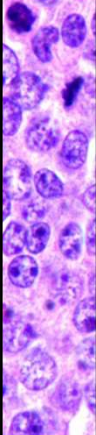


Mom's Third 25th Birthday - Joy

“The greater part of our happiness or misery depends upon our dispositions, and not upon our circumstances.”
--Martha Washington

“Happiness cannot be traveled to, owned, earned, worn or consumed. Happiness is the spiritual experience of living every minute with love, grace and gratitude.”
--Carol Markiewicz Power

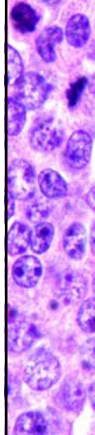




Ocular Melanoma


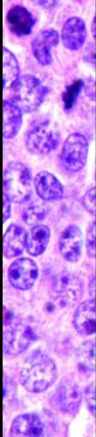
Cats & Dogs

- Limbal melanocytomas
- **Limbus** – where cornea meets sclera
- Most common in superior quadrants
- **Gonioscopy required to distinguish from scleral metastasis of melanoma**
- Removal not indicated if benign behavior
- **Growing lesions removed by an ophthalmologist (may require graft)**



Ocular Melanoma

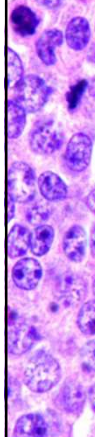
Cats

Ocular Melanoma

Dogs – uveal melanocytoma

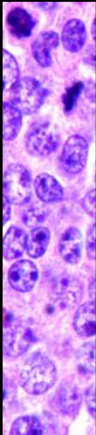
- The vast majority are benign (90%)
- Only 50% of those classified by histopath as malignant actually metastasize after removal of the eye
 - Mortality of uveal melanoma 5%
- Most arise from the anterior uvea
- Choroidal and limbal melanomas less common
- Freckles and nevi also common




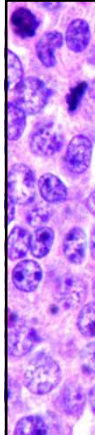
Ocular Melanoma

Dogs – uveal melanocytoma

- can destroy the globe and cause glaucoma
- Removal of the eye is 95% curative
- Same recheck schedule as for cats
- Same treatment
- Better prognosis (95% cure rate)
- **Staging prior to enucleations is indicated, but low yield**



Mom's Third 25th Birthday - Family

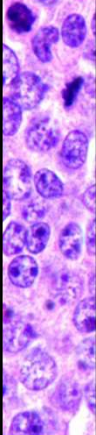
Mom's Third 25th Birthday - Family

"Find your way to swing the pendulum in the direction of love. ...Imagine the difference if we each purposefully love a little more."

--Ben Carson

"People will forget what you said. People will forget what you did. But people will never forget how you made them feel."

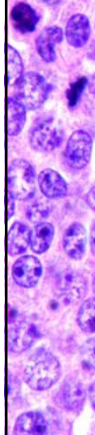
Maya Angelou



Ocular Melanoma

Dogs

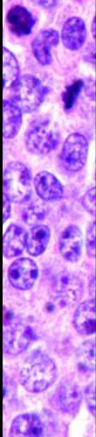
- **Limbal melanocytoma**
 - GSD and Labrador predisposed
 - Usually superior quadrant
 - Growth rate variable
 - Rarely affect vision or cause glaucoma
 - Often accompanied by margin of corneal lipid dystrophy
 - Gonioscopy can evaluate for local invasion in rare case of malignancy



Ocular Melanoma


Dogs

- **ocular melanocytoma**
 - Usually bilateral
 - Older terriers
 - Insidious panuveal proliferation
 - Hyperpigmentation of the iris
 - Free floating cells in the anterior chamber and adhering to the anterior lens
 - Progresses to graying of the sclera
 - Can result in glaucoma
 - Almost never metastasizes



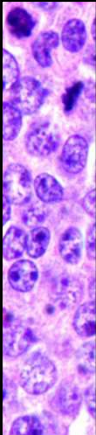
Ocular Melanoma

Dogs




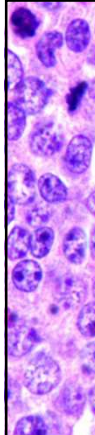

Ocular Melanoma

Dogs

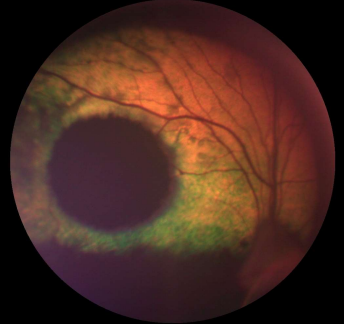
Ocular Melanoma

Dogs


Ocular Melanoma

Dogs



Percy


- 10 year old neutered male Persian cat
- CC – left eye has been dilated since applying Advantage 2 months ago
- Owner wants to file a complaint with Bayer



Percy

Exam

- Enlarged submandibular lymph nodes
- Fundic exam unremarkable
- PLR almost absent OS, normal OD




Percy



Percy

DDx - anisocoria


- Unilateral oculomotor nerve disease
 - Forebrain disease
- Iris disease
 - Previous trauma and synechiae
 - Iris freckles or iridial cysts
 - Iris melanoma




Percy

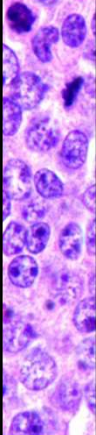
Diagnostic Plan

- Neurologic exam normal except abnormal PLR
- FeLV ELISA negative
- Chest x-rays and abdominal US
- Lymph node aspiration



Mom's Third 25th Birthday – Love Work






Mom's Third 25th Birthday – Love Work

Some of us need to be successful in order to be happy. Others need to be happy in order to be successful.

Some of us enjoy work for pay as part of a full life. Others work for pay in order to enjoy their life.


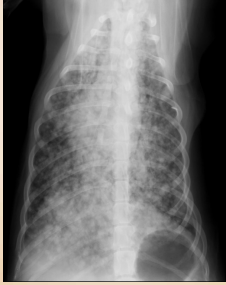
If you can manage to find joy wherever you happen to be, I think you've got it licked.

--Wendy Blount





Percy

Thoracic radiograph




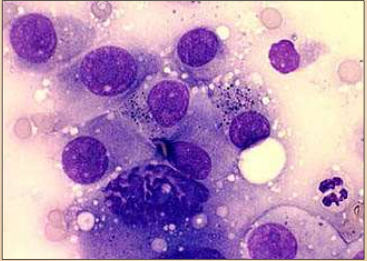
Percy

Liver ultrasound



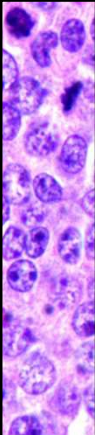
Percy

Lymph node Cytology



Percy

- To this day, the owner believes Advantage caused the cancer
- Against our advice, the owner called Bayer, FDA and EPA to report an adverse reaction
- When her complaints went nowhere, she conjured up conspiracy theories



Summary

- [PowerPoint](#)
- .pdfs of [PowerPoint – 1 & 6 slides](#) per page

Laboratory Information:

- MSU – [Immunohistochemistry Form](#)
- MSU – [Molecular Pathology Fees](#)
- MSU – [Gross Pathology Fees](#) (Melanoma Panel)
- MSU - [Melanoma Prognostic Panel Form](#)
- MSU – [List of Pathology Panels](#)

Summary

Vet Handout: [MSU – Melanoma Prognostic Panel](#)

Client Handout: [Melanoma](#)

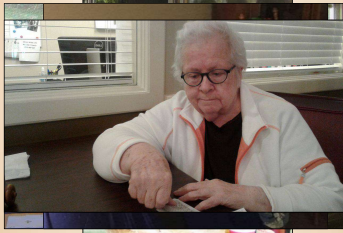
Drug Handouts

- [Cimetidine](#)
- [Piroxicam](#)
- [Merial - Oncept® Melanoma Vaccine](#)


Hidden Slides

- Digital Melanoma Study
- Ocular melanocytomas
- Lyrics – “I’m Not Gonna Miss You”

She’s Not Gonna Miss Me



She’s Not Gonna Miss Me



Glen Campbell (April 22, 1936 – August 8, 2017)

I’m Not Gonna Miss You

I’m still here but yet I’m gone.
 I don’t play guitar or sing my songs.
 They never defined who I am,
 the man that loves you till the end.
 You’re the last person I will love.
 You’re the last face I will recall.
 Best of All,
 I’m Not Gonna Miss You.

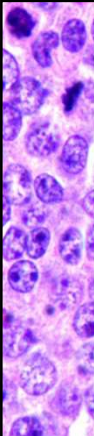
I’m Not Gonna Miss You

I’m never gonna hold you like I did,
 or say, “I Love You,” to the kids.
 You’re never gonna see it in my eyes.
 It’s not gonna hurt me when you cry.
 I’m never gonna know what you go
 through.
 All the things I say or do,
 All the hurt and all the pain,
 One thing selfishly remains.
 I’m Not Gonna Miss You.

Acknowledgements

Robert L. Peiffer, Jr., DVM, PhD, DACVO

- School of Medicine, Univ North Carolina Chapel Hill, NC
- **Philip Bergman, DVM, MS, PhD, ACVIM (Oncology)**
 Director, Clinical Studies (VCA)
 Oncologist, Ketonah-Bedford Vet Center
 Bedford Hills, NY
 VetFolio Oncology Certificate Program



Acknowledgements

Hazelyn Patterson, DVM and Kenneth S. Latimer, DVM, PhD

- Department of Pathology (Latimer)
CVM, The University of Georgia Athens, GA

VDIC – Veterinary Diagnostic Imaging Center

- Clackamas, OR

Claudia Barton, DVM, ACVIM

- TAMU CVM



Acknowledgements

Zachary Wright, DVM, ACVIM (Oncology)
Animal Diagnostic Clinic, Dallas TX

Michael H. Goldschmidt, BVMS & Patricia McManus, VMD, PhD

- University of Pennsylvania School of Veterinary Medicine



Acknowledgements

Maristavet.com

TheCatSite.com

VeterinaryVision.com

VetBook.org

EyeVet.info

ScienceDirect.com

FelineDiabetes.com

PetMD.com