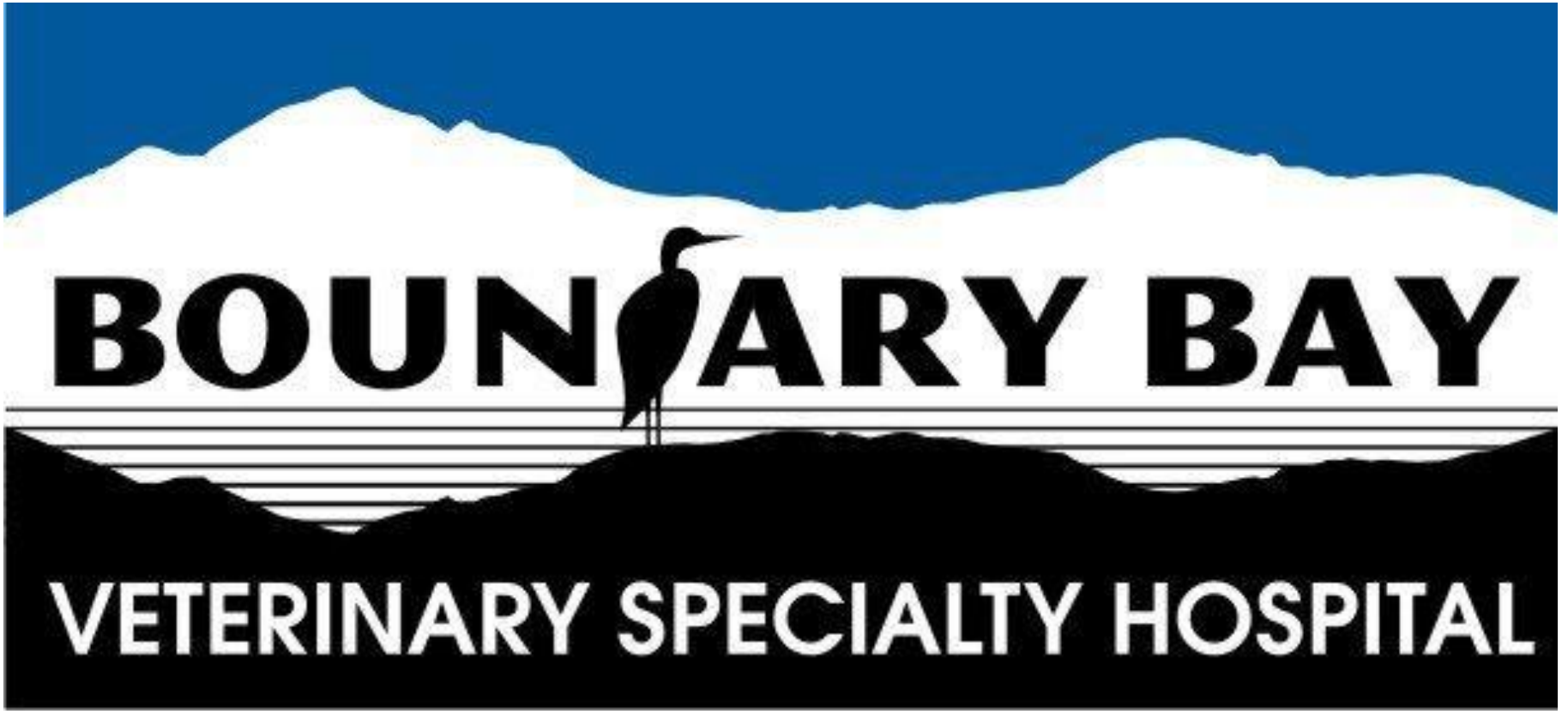

Oral Tumors

Chamisa Herrera, DVM, MS, DACVIM

Housekeeping

- Session 2: 90 minutes
  - Anytime: “Questions for Speakers” on the left of HOME screen
  - Mini #1: Oral Tumors- Questions at 10:40am
  - Mini #2: Mast cell Tumors- Questions at 11:20

"I'd better run some tests... It could be cancer."

Agenda

- Tumors
  - Epulides/Ameloblastoma
  - Squamous Cell Carcinoma
  - Fibrosarcoma
  - Melanoma
- Topics
  - Tumor behavior
  - Staging
  - Medical/adjunctive therapies
  - Prognostic factors
  - Prognosis

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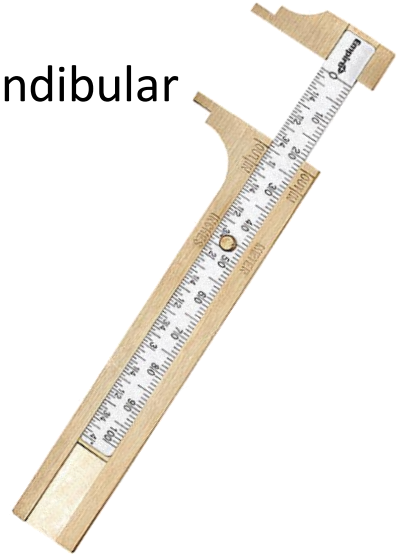
Presentation and Staging

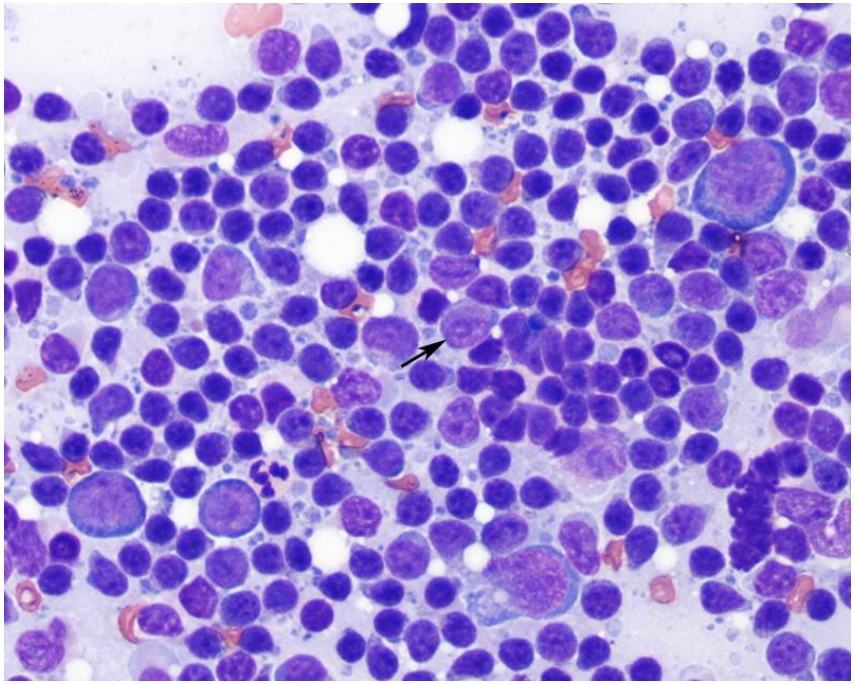
9yr MC- Duke

- Cries when eating
- Won’t play fetch

Diagnostic Techniques and Work-Up

- Suspect malignancy? First steps!
  - #1- Document tumor size and location
  - #2- FNA of mandibular lymph nodes (even if normal)
    - Surprise diagnosis!
    - 55% of patients with LN mets had metastasis to mandibular LN
    - Other potentials for regional LN mets
      - Parotid
      - Medial retropharyngeal
  - #3- Thoracic radiographs +/- AUS






R
JC

Staging

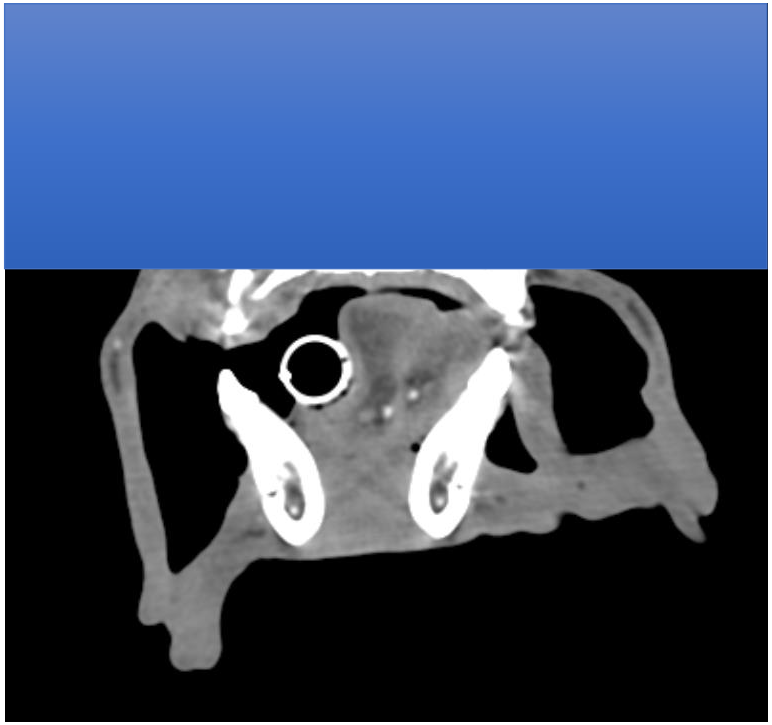
Tumor (T)	Lymph Node (N)	Distant Mets (M)
• 1 (I): <2cm • 2 (II): 2-4cm • 3 (III): >4cm	• 0- none • 1- moveable ipsilateral • 2- moveable contralateral • 3- fixed	• 0- none • 1- distant mets
• a- no bone invasion • b- bone invasion	• a (-) • b (+)	• Stage IV- Distant mets

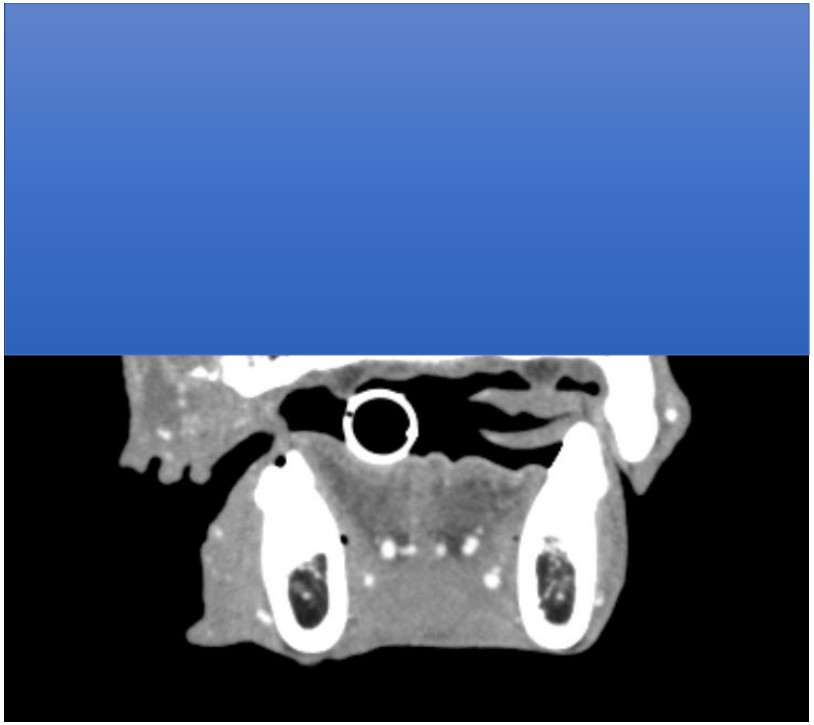
Now What?

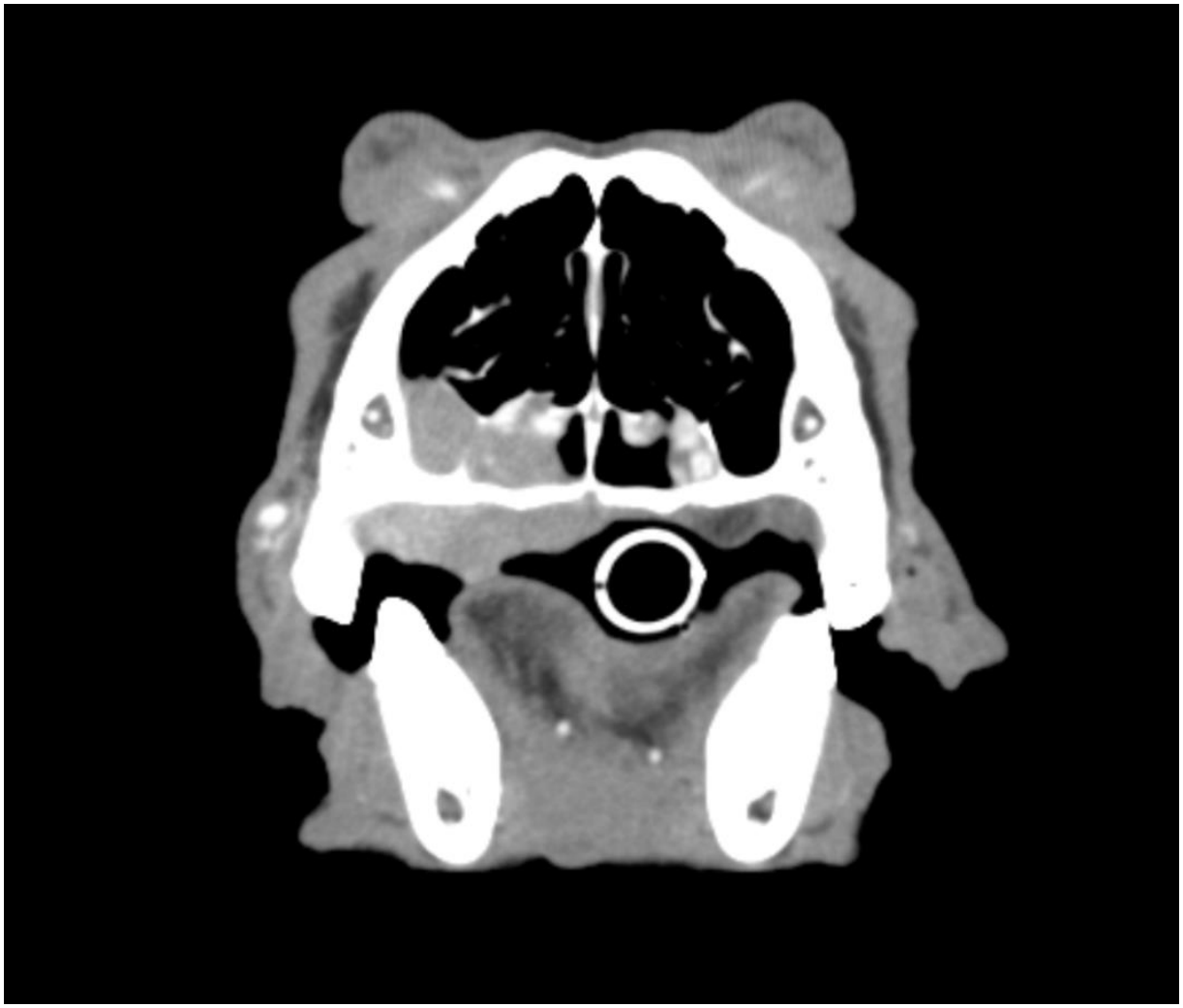
- Imaging
  - Dental radiographs- Rostral tumors, mandibular tumors
  - CT for any maxillary, palate, caudal mandible

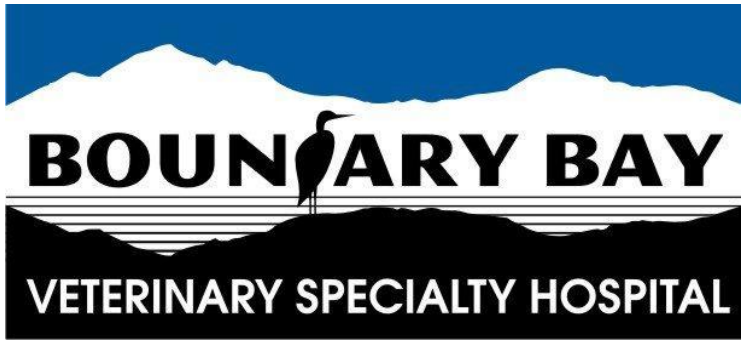
- Take advantage of anesthesia → Biopsy!
  - Plan carefully to avoid tumor seeding → oral approach
  - Exophytic or ulcerated- may not need anesthesia

- What about cytology of the tumor?
  - Not very useful typically
  - Special stains?



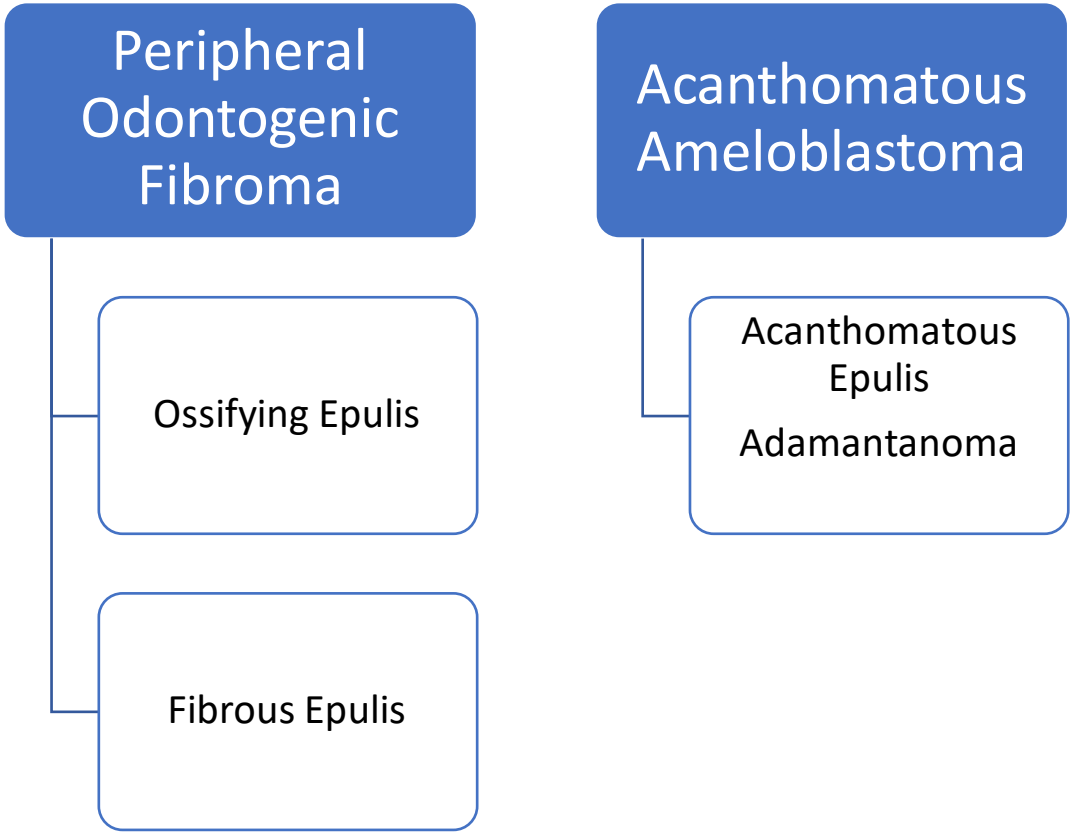






Specific Tumor Subtypes

Acanthomatous Ameloblastoma and Epulides


Peripheral Odontogenic Fibroma
Ossifying Epulis
Fibrous Epulis
Acanthomatous Ameloblastoma
Acanthomatous Epulis
Adamantanoma

Peripheral Odontogenic Fibroma

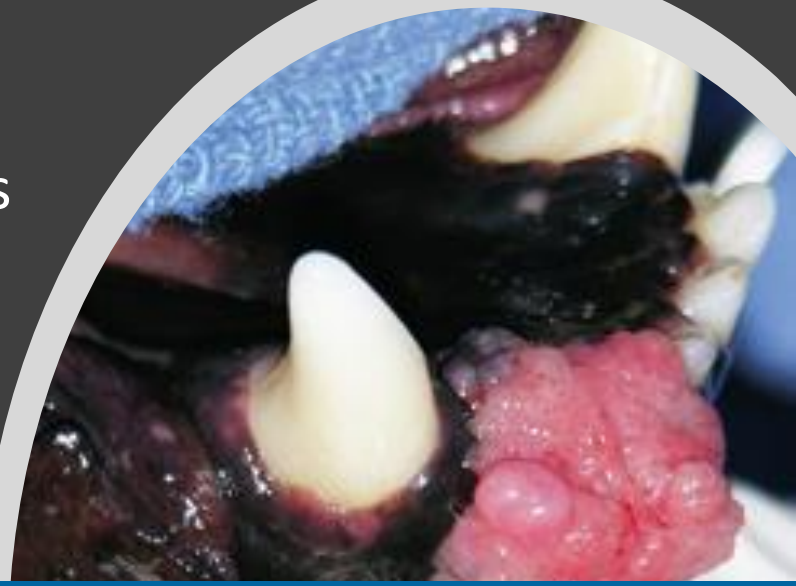
- Risk Factors
  - Common in dogs
  - Uncommon in cats

- Behavior
  - Slow growing firm masses covered by intact epithelium
  - Predilection for maxilla rostral to 3rd premolars

- Treatment: 0-17% recurrence when removed *without* bone margin

Acanthomatous Ameloblastoma

- Locally aggressive → invade bone
- 7-10 years
- Shetland and Old English Sheepdogs
- Rostral mandible is most common
- DO NOT metastasize

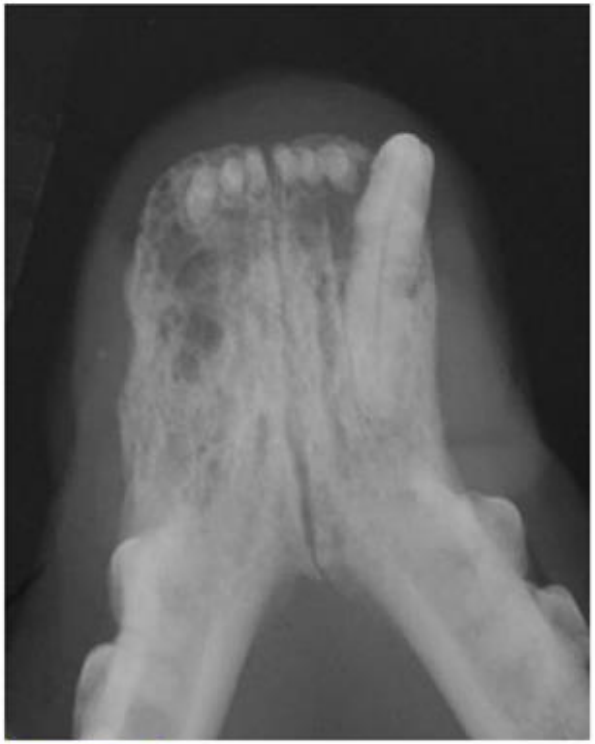


Acanthomatous Ameloblastoma

- Surgery
  - Must include a bone margin, recurrence <5%
- Radiation
  - 3 year progression free survival of 80%
    - 8-18% recurrence
    - Recurrence 8X more likely for T3 tumors than T1/T2
  - 12 x 4 Gy
- Intralesional Bleomycin
  - Weekly or bimonthly injections
  - 6/7 complete response rate (Kelly VCO 2010)
  - Not this effective in my experience

Squamous Cell Carcinoma

Squamous Cell Carcinoma



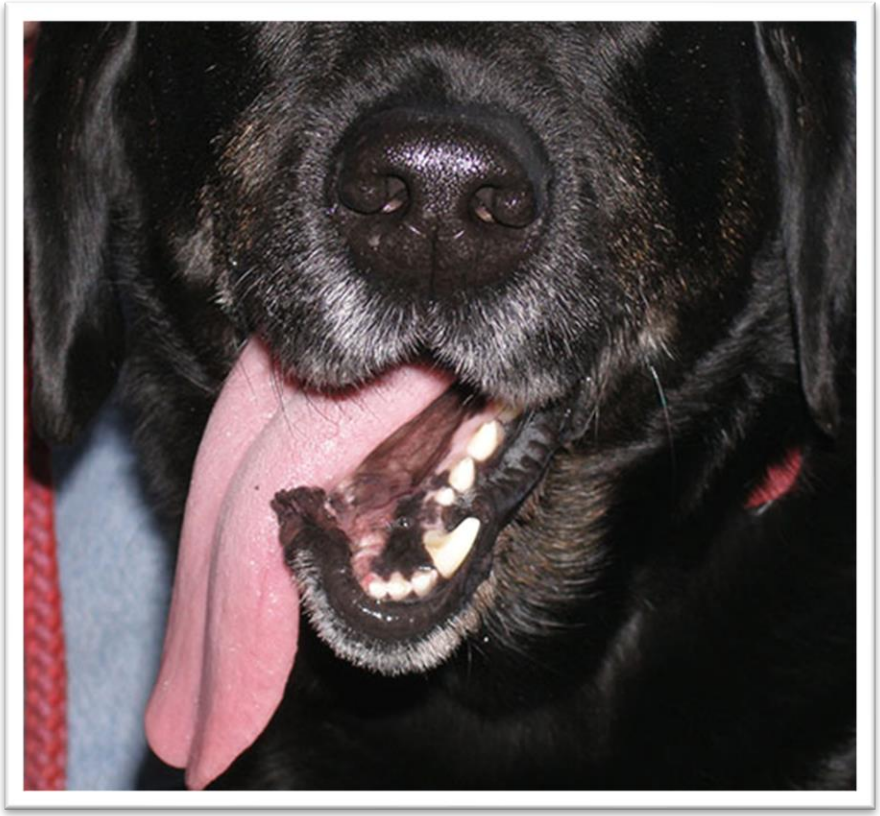
From: Withrow and MacEwen's Small Animal Clinical Oncology 5th Edition

FIGURE 22-4 An intraoral radiograph of the rostral mandible of a cat with a SCC. Note the extensive, ill-defined bone lysis that is very common in cats with this type of tumor.

- Common
  - Most common oral tumor of cats
  - Second most common oral tumor of dogs
- Behavior
  - High rate of bone invasion
  - Uncommon Metastasis
    - <20%
    - Canine Tonsillar SCC* is highly metastatic (73%)

Canine Squamous Cell Carcinoma

- Surgery
  - Location, Location, Location
    - Mandibulectomy: 10% recurrence, survival 19-26mo
    - Maxillectomy: 29% recurrence, survival 10-19mo
    - Tonsil: almost never useful
- Radiation
  - Alone: 15-16mo
  - Adjunct to surgery: 34mo
  - Size matters!
    - T1- 68 mo
    - T2- 28 mo
    - T3- 8 mo
    - Tonsil: 10% 1 year survival



Feline- Squamous Cell Carcinoma

- Overall poor- MST 1-3mo

- Surgery- Location! Location!
  - Mandibulectomy +/- Radiation: 12-14mo
    - Rostral: 30mo
    - Hemi: 7mo
  - Maxillectomy: Crazy Loco

- Radiation
  - Overall not effective
  - Radiation (14 tx in 9 days) + Carboplatin= MST 5.5mo

Squamous Cell Carcinoma

- Chemotherapy
  - Tonsillar- Radiation + Chemotherapy improves survival

- Piroxicam
  - Cats: No improvement in most studies
  - Dogs:
    - Piroxicam alone: 17% response
    - Cisplatin + Piroxicam: 56% response, 41% renal toxicity
    - Carboplatin and Piroxicam: 57% complete response

Fibrosarcoma

Fibrosarcoma

- Moderate frequency of occurrence
  - 2nd most common feline tumor
  - 3rd most common canine tumor

- Risk Factors
  - Dogs: Large breed, early senior years (7-8)
    - Goldens
    - Labs

Fibrosarcoma

- Behavior
  - Locally aggressive
  - Moderate metastatic rate: 20- 30%
    - Lungs
    - Regional lymph nodes

Fibrosarcoma

- BEWARE: Biologically high grade, histologically low grade
  - “High-Low”
  - Location often palate or maxillary arcade between canine and carnassial tooth
  - Golden Retrievers (52%)

Fibrosarcoma

- Surgery
  - Dogs
    - Overall rule: 50% recurrence, MST 1 year
  - Cats:
    - Mandibulectomy: 28mo (n= 5)
- Radiation alone
  - 7 mo
- Radiation + surgery
  - 32% recurrence, MST 18-26mo
  - Size
    - T1- 45mo
    - T2- 31mo
    - T3- 7mo

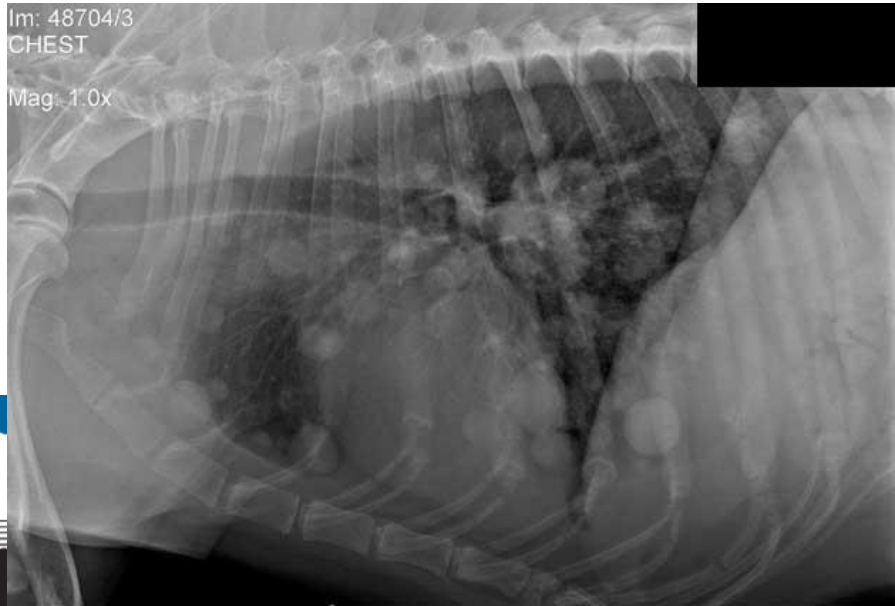
Melanoma

Malignant Melanoma

- Predispositions- smaller body weight breeds
  - Cocker Spaniel
  - Miniature Poodle
  - Anatolian Sheepdog
  - Chow Chow
  - Gordon Setter
  - Golden

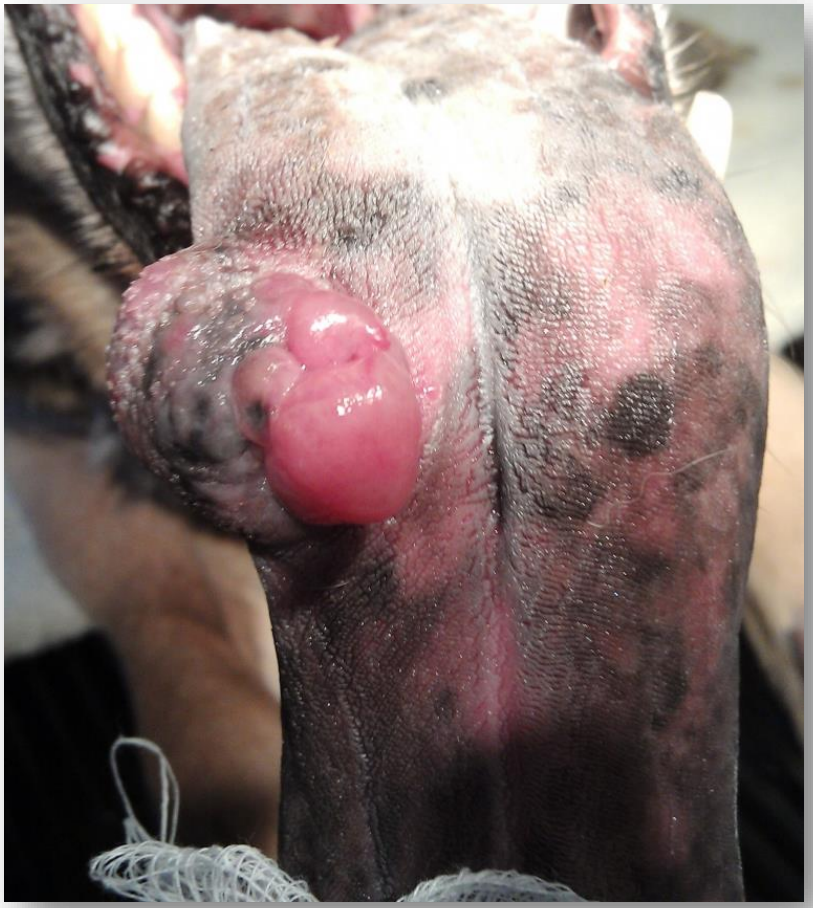
Malignant Melanoma

- Behavior
  - Highly metastatic (>2/3)
    - Lungs
    - Lymph nodes
      - 40% of dogs with normal lymph nodes had metastasis
      - 49% with enlarged lymph nodes did not had metastasis
  - Highly immunogenic
- Cutaneous melanoma
  - Different! Often benign



Malignant Melanoma

- Treatment- Surgery
  - Overall 9-12 mo
    - Stage I: 18 months
    - Stage II: 6 months
    - Stage III: 3 months
  - Location Matters!
    - Worse: Maxilla, Caudal
    - Better: >18mo
      - Tongue
      - Lip

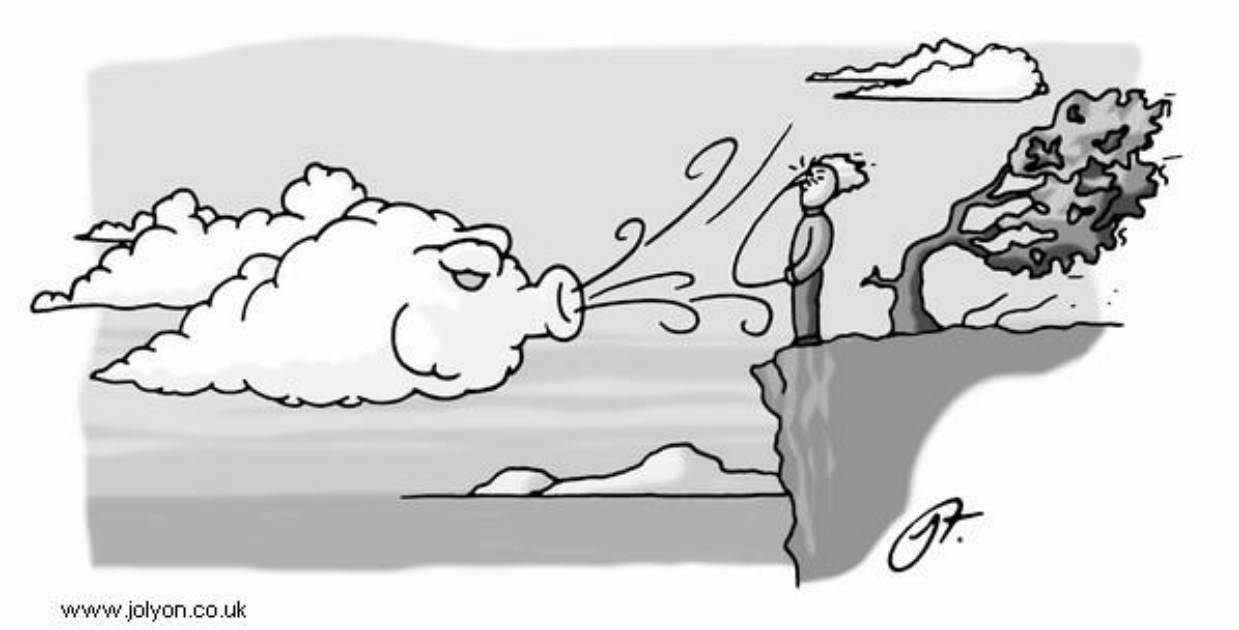


Malignant Melanoma

- Treatment- Course Fractionated Radiation
  - Response Rates
    - Dogs: 83-100%; 70% Complete
    - Cats: 60%
  - Protocols- typically 3-8 total treatments
    - 3x 8 Gy; 4 x 9Gy; 6 x 6 Gy; 8 x 6 Gy
  - Side Effects
  - Prognosis
    - Stage I: 19mo
    - Stage II and III: 7 mo

Malignant Melanoma

- Chemotherapy
  - Cisplatin
  - Carboplatin
  - Melphalan



Malignant Melanoma

- Melanoma (Oncept) Vaccine
  - Mechanism- See Intro
  - Procedure:
    - q2 weeks x 4
    - then q6 months
  - Client Cost: $700-900/vx

Oncept- Literature Review

- 2011 Grosenbaugh
  - 111 dogs (58 prospective, 53 historical)
  - Stage I-III: >900 days, Stage IV: 8 mo
- 2013 Ottnod: 45 dogs
  - Dogs that received the vaccine did not achieve a greater progression-free survival, disease-free interval, or MST
- 2016 Treggiari:
  - Dogs with locoregional control and vaccine (n=32), MST 335 days
- 2017 Verganti
  - Dogs with stage I-III (n= 56) and locoregional control had MST of 455 days

Melanoma

- Summary
  - Surgery: 9-12 mo
    - Stage I: 17 to 18 months
    - Stage II: 5 to 6 months
    - Stage III: 3 months
  - Radiation: 7-12 mo
    - Stage I: 19mo
    - Stage II and III: 7 mo
- Vaccine only after local control
  - Exception?
- Chemotherapy?

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Oral Tumors Review

Prognostic Factors

- Size/Stage
- Location
- Tumor Type
  - Could we consider radiation as a good alternative?
  - Other Adjuvant therapy?

- Surgery is always best if possible
  - Need a *gross* bone margin (≥1-2cm)
    - Exception: Peripheral odontogenic fibroma
  - Histopathology Report
    - *Histologic* margins complete? How close?
      - Worry if <3mm
      - Ideal >5-10mm
    - What is the mitotic index?
      - Melanoma
    - Were lymph nodes resected? Were they positive?

Surgery- Done!
Do I need adjuvant therapy?

- Yes → Radiation
  - Incomplete margins
  - Fibrosarcoma- clean but close histologic → full course
  - Another tumor that is close (<3-5mm) → consult
- Yes → Chemotherapy
  - Questionable- consider for OSA, tonsillar SCC, any stage IV
- Yes → Immunotherapy
  - Melanoma that is locally controlled- Oncept melanoma vaccine

Doc- I won't do that surgery!

- Tumors where radiation is a good alternative
  - Canine SCC- Fine fractionation
  - Melanoma- Course fractionation
  - Acanthomatous ameloblastoma- Fine fractionation

- Tumors where we can get creative
  - Tonsillar SCC
  - Acanthomatous Ameloblastoma

Palliative Care

- Without treatment → Pain!
- Most tumors ~2mo
  - How much pain do owners tolerate?
- Palliative Care
  - Pain control
    - NSAIDS- Piroxicam
    - Prednisolone
    - Opioids
  - Control secondary infections
  - Palatable food
  - Feeding tube?

We are only a phone call away!

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Questions?

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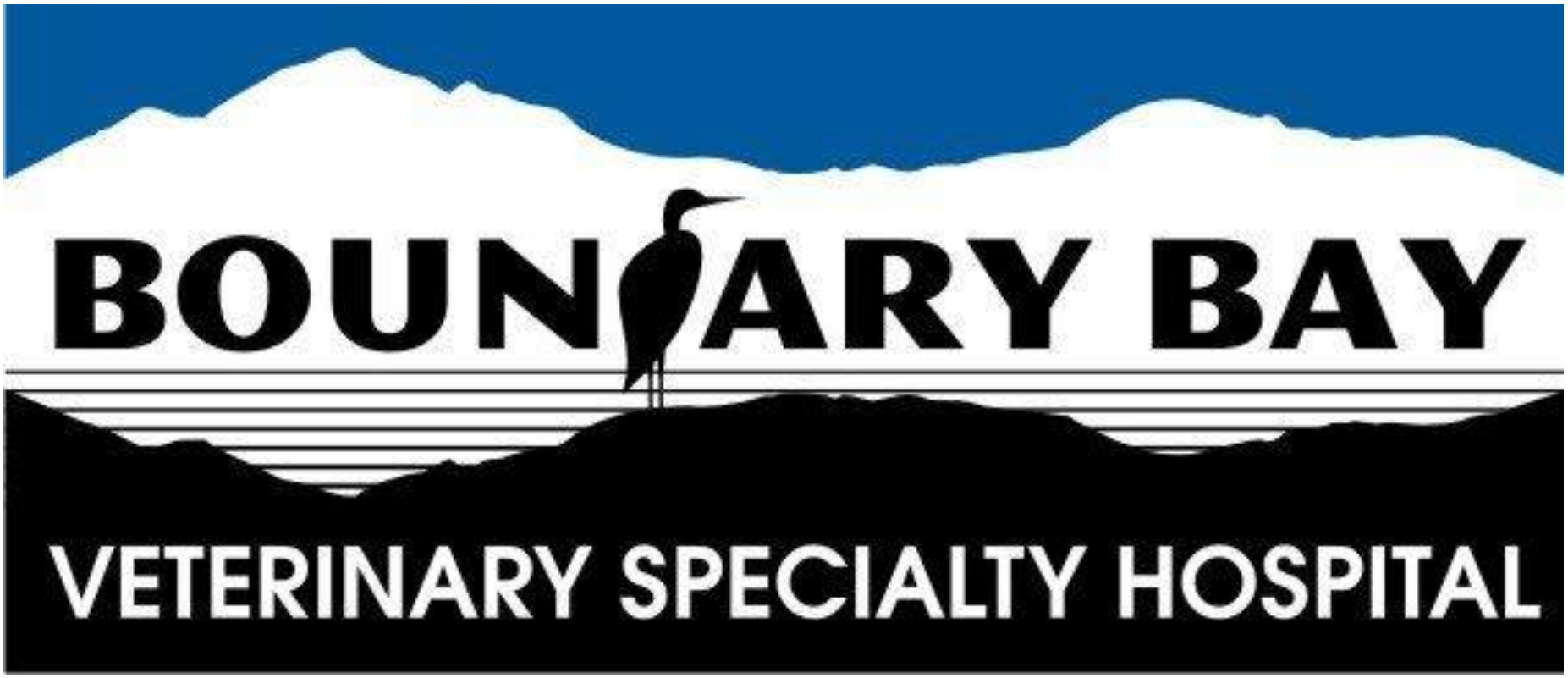
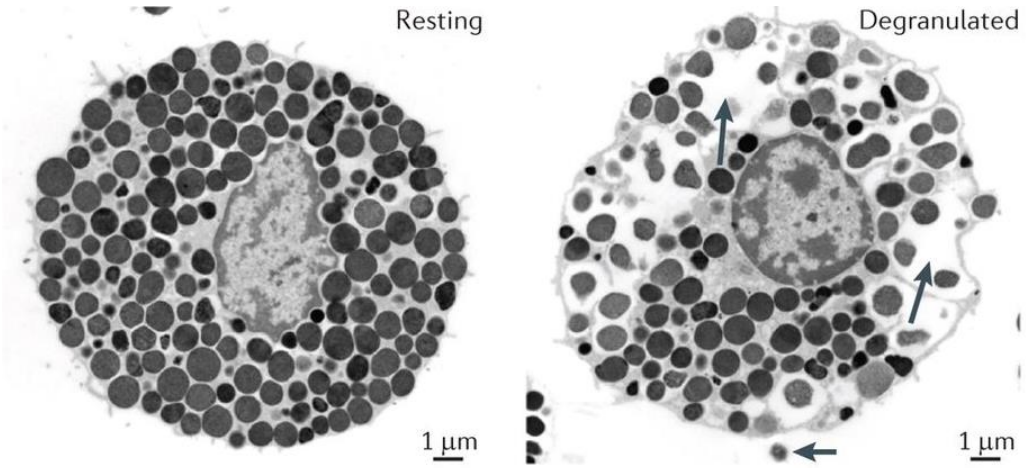


Mast Cell Tumors

What is a mast cell?

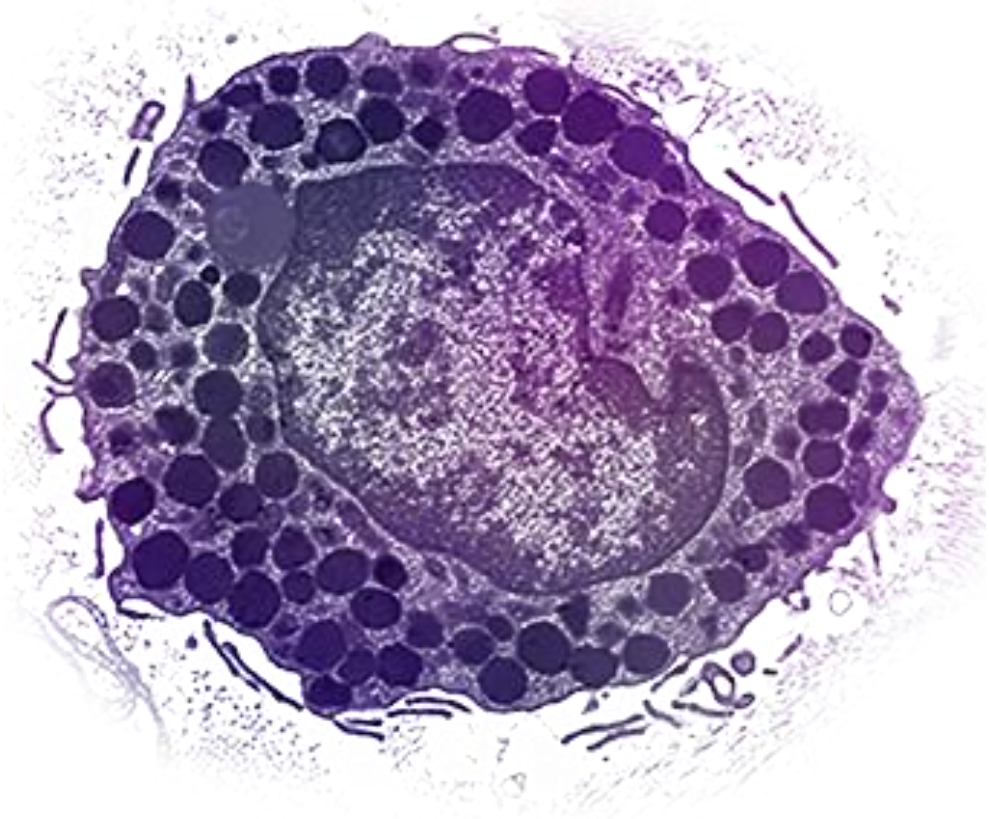
- A type of granulocyte
- Found in all vascular tissue except retina and CNS
- Located at junction between host and external environment



Nature Reviews | Immunology

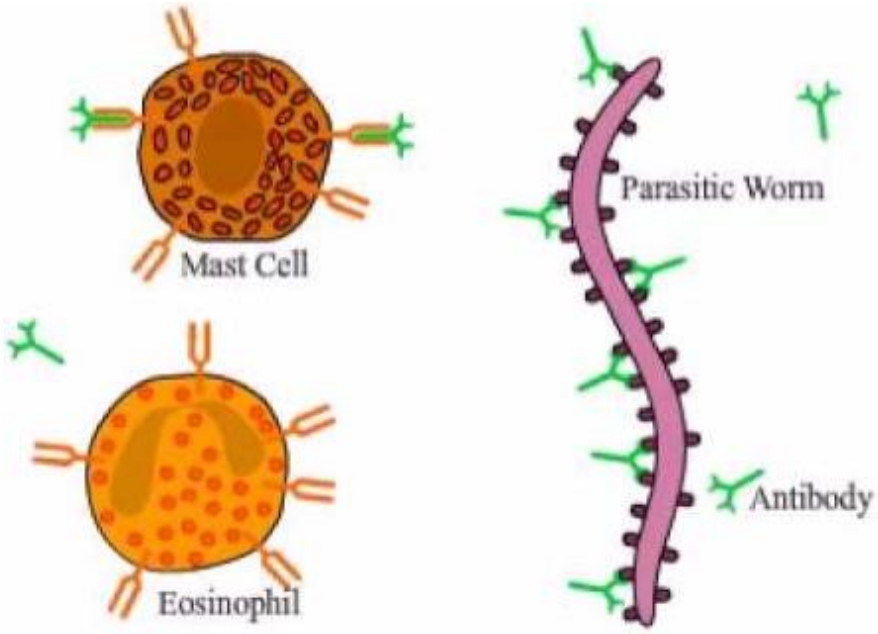
What is a mast cell?

- 50-200 granules
  - **Histamine**
  - **Heparin**
  - **Proteases**
  - **TNF**
  - Chondroitin
  - Prostanoids
  - Leukotriene

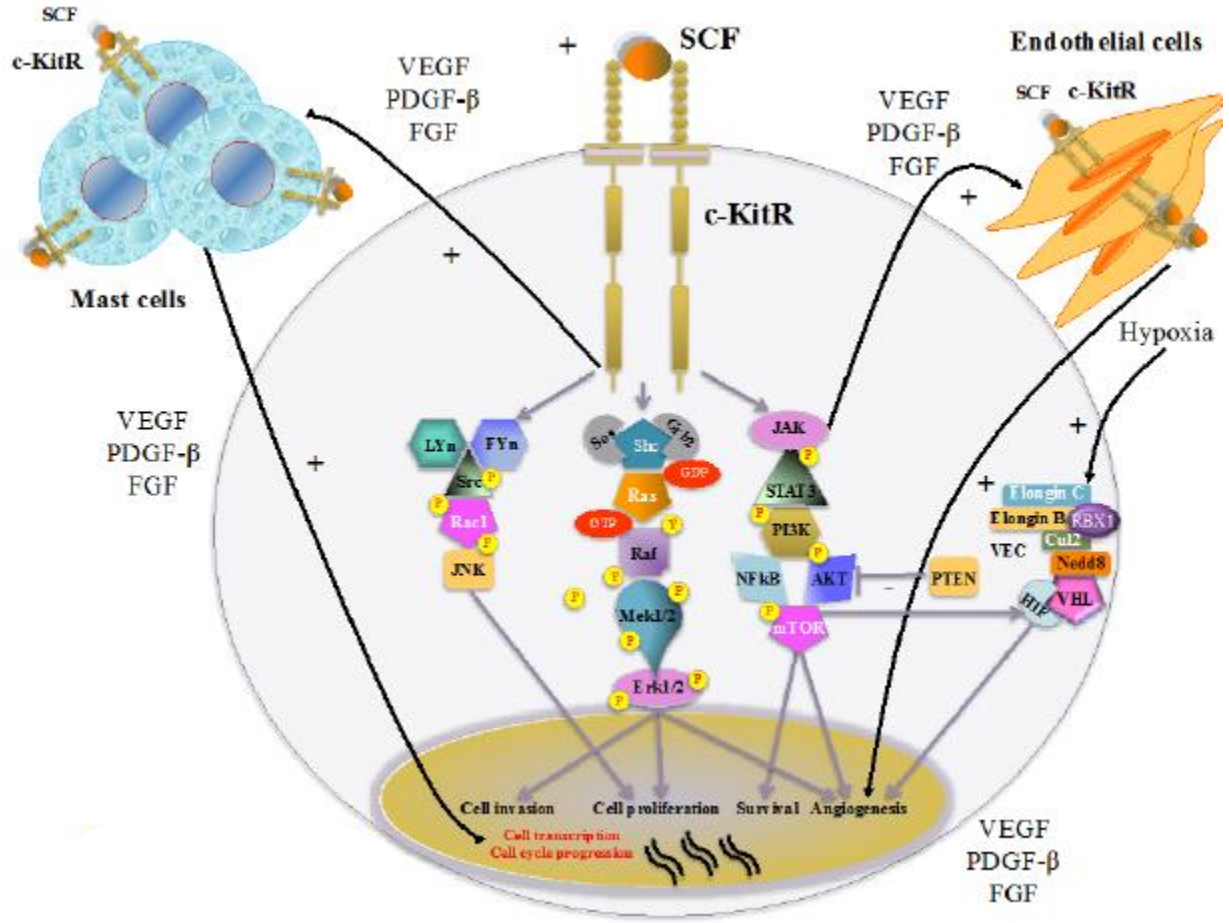


Role of Mast Cells

- Parasite elimination
- Angiogenesis
- Wound Healing
- Bone growth/remodeling



Mast cell proliferation



Mast cell tumor

- AKA
  - Histiocytic Mastocytoma
  - MCT
  - Mast Cell Sarcoma
  - Systemic form: Mastocytosis

- 16-21% of all cutaneous tumors

Mast cell tumor

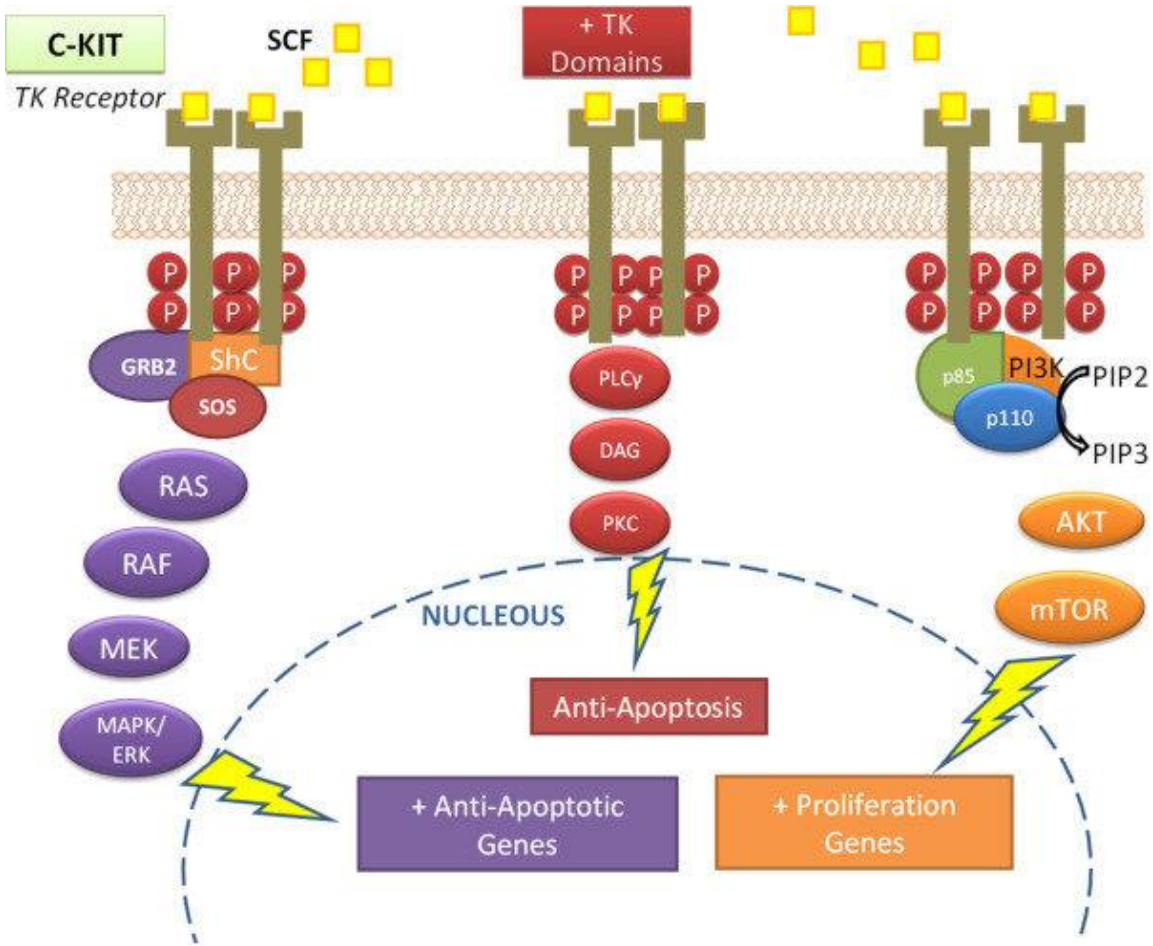
- Breed Predispositions
  - **B**oxers
  - **B**ostons
  - **B**ulldogs
  - **B**eagles
  - Pit **B**ull
  - **Pugs**
  - Labrador
  - Schnauzer
  - Rhodesian Ridgeback
  - Weimaraner
  - *Shar-peis → aggressive MCTs*

MCT behavior

- Locally aggressive
- Metastatic rate is *generally* grade dependent
  - Local lymph node → liver/spleen → bone marrow/blood

Pearl: Stage the lymph node for every case!

Pearl: Lung is unusual location of metastasis



25-30% intermediate and high grade MCTs have a C-kit mutation

Presentation: *Generalities*

- Low grade
  - Solitary
  - Slow growing
  - Small
  - Several month or longer history

Presentation: *Generalities*

- Low grade
  - Solitary
  - Slow growing
  - Small
  - Several month or longer history
- High grade
  - Rapidly growing
  - Large
  - Ulcerated
  - Inflamed
  - Visceral mets- anorexia, vomiting, melena

Prognostic Factors: GRADE (Patnaik)

I

- Typically don't met
- Can be cured with wide excision

II

- Unpredictable- some act like low grade, some act like high grade
- If mitotic index >5 → treat like high grade

III

- High rate of metastasis
  - Lymph nodes, liver, spleen
- Usually best treated with wide excision AND chemotherapy (<1yr)

Prognostic Factors: GRADE (Patnaik)

I

- Typically don't met
- Can be cured with wide excision

II

- Unpredictable- some act like low grade, some act like high grade
- If mitotic index >5 → treat like high grade

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- Typically don't met
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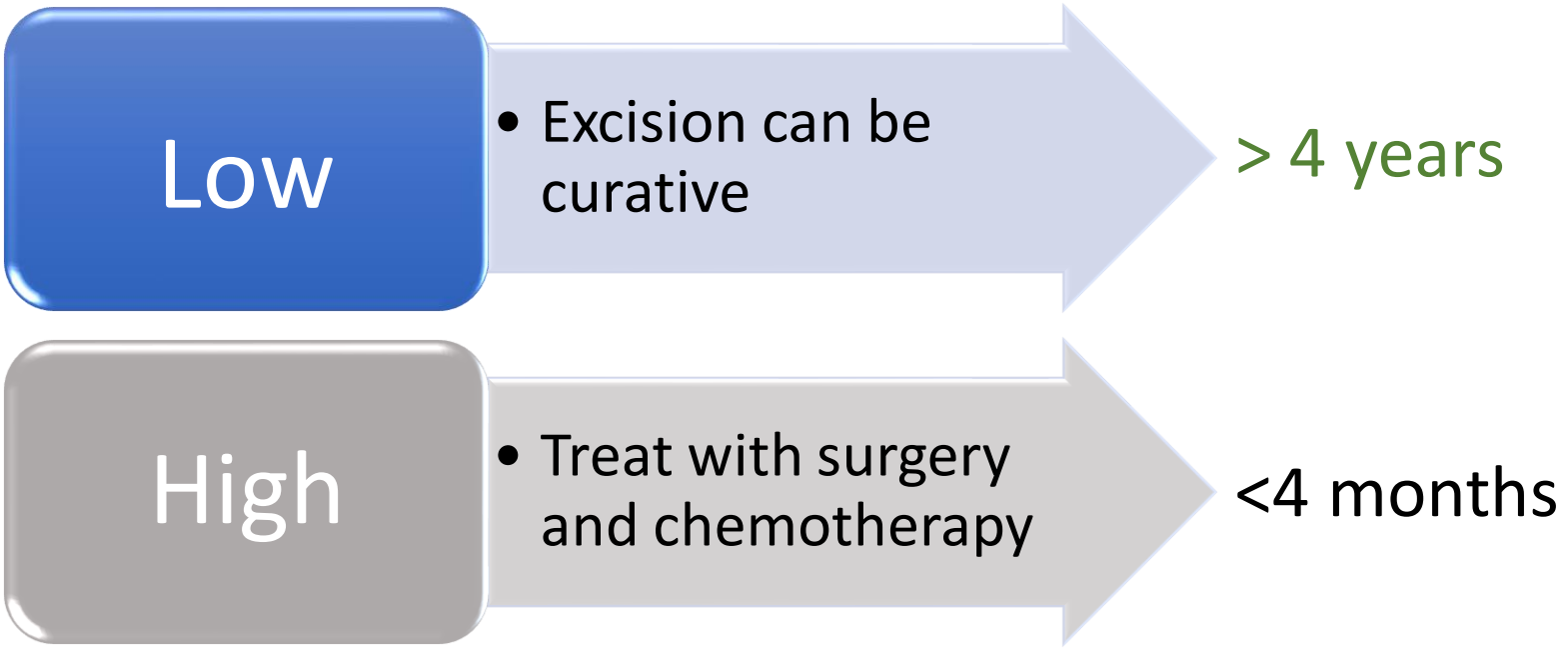
- Unpredictable- some act like low grade, some act like high grade
- If mitotic index >5 → treat like high grade

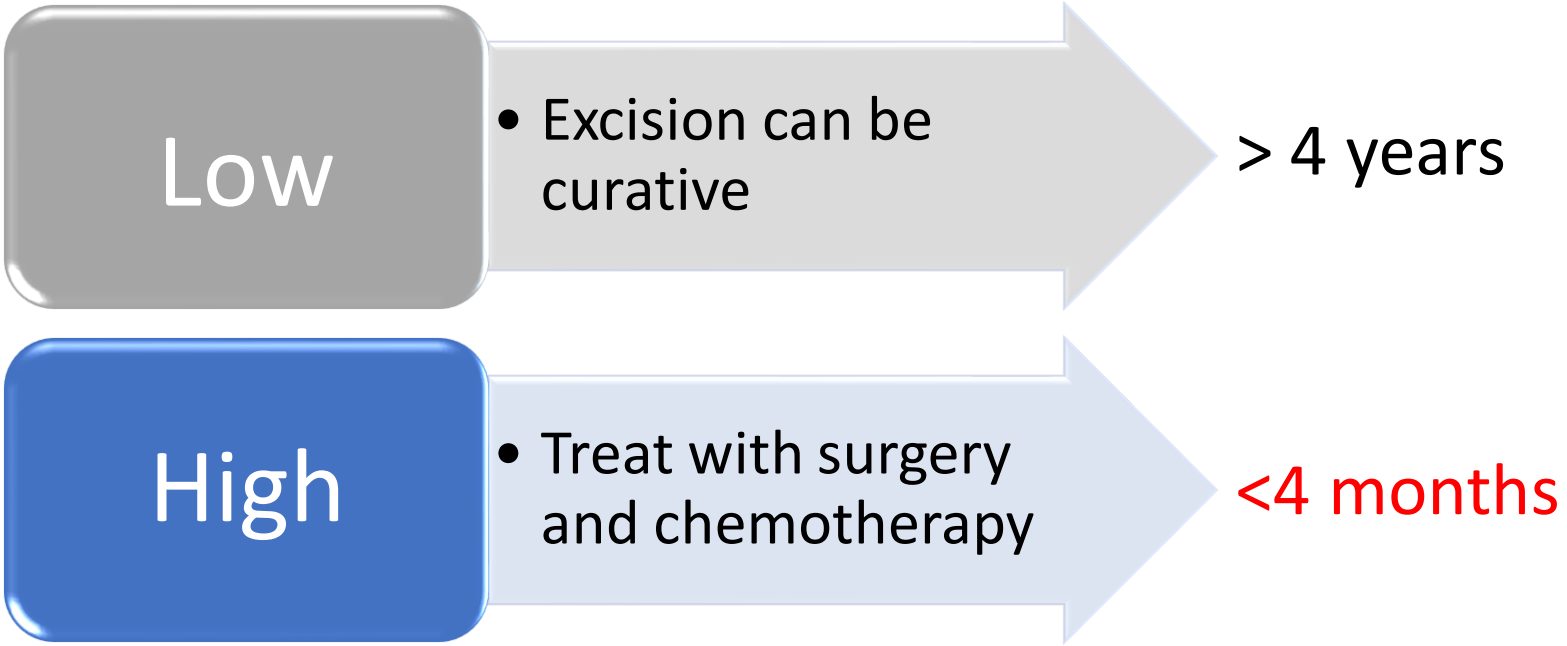
III

- High rate of metastasis
  - Lymph nodes, liver, spleen
- Usually best treated with wide excision AND chemotherapy (<1yr)

Prognostic Factors: GRADE (Kiupel)

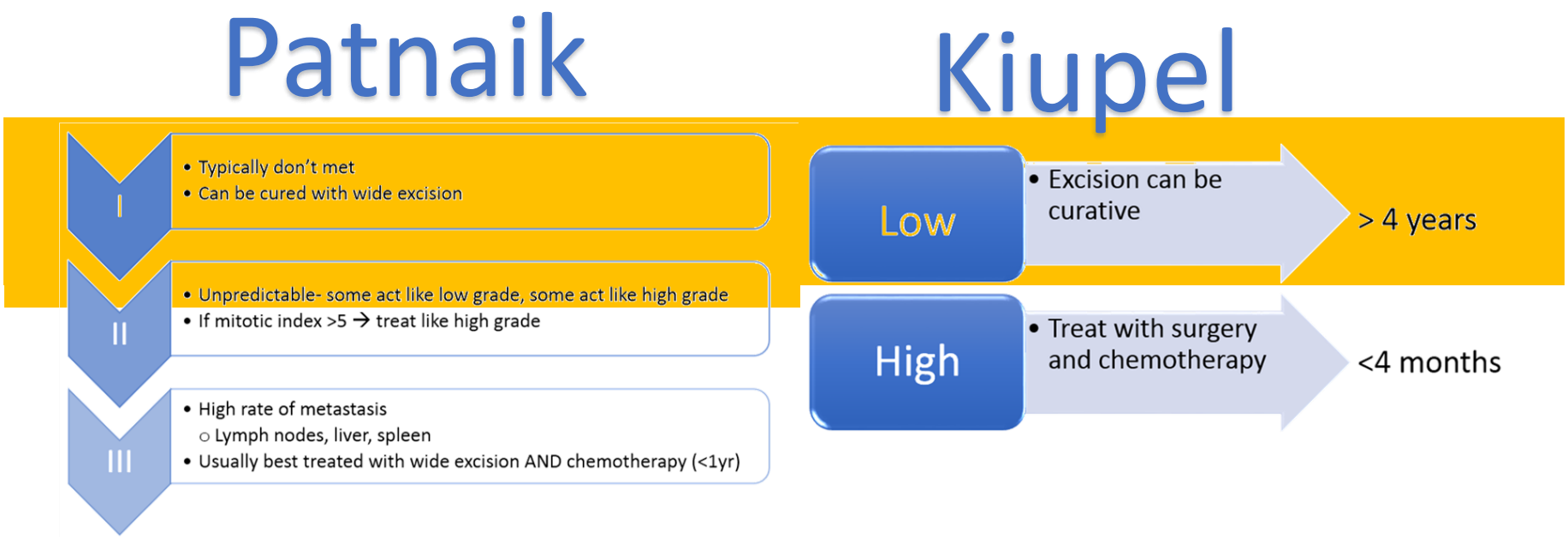


Prognostic Factors: GRADE (Kiupel)



- ≥7 mitosis/10 HPF
- ≥3 multinucleated cell/10HPF
- ≥3 bizarre nuclei/10HPF
- Karyomegaly

Grade Summary

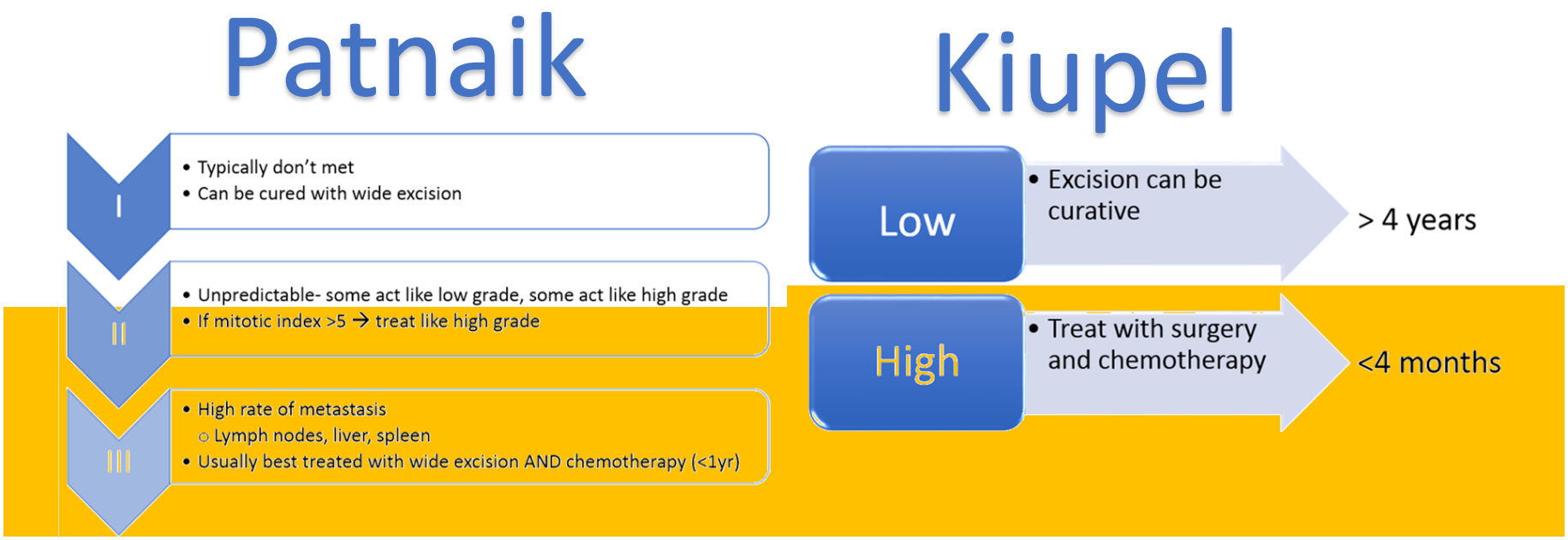


Low Grade= grade I= low grade II (MI<5)

Can be cured

Caution with low grade II's → some don't follow rules, most do

Grade Summary



High Grade= high grade II = grade III
Recommend local control AND chemotherapy
Generally <1 year with multi-modal treatment

Prognostic Factors: Location

- Worse
  - Preputial/Inguinal
  - Subungual
  - Mucocutaneous
  - Viscera: Grave

Prognostic Factors: Location

- Worse
  - Preputial/Inguinal
  - Subungual
  - Mucocutaneous
  - Viscera: Grave
- Better
  - Subcutaneous (MI <4= ☺)

Prognostic Factors: Location

- Worse
  - Preputial/Inguinal
  - Subungual
  - Mucocutaneous
  - Viscera: Grave
- Better
  - Subcutaneous (MI <4= ☺)
- Special: Muzzle

Prognostic Factors: Stage

I	One tumor confined to the dermis without lymph node involvement
II	One tumor confined to the dermis **with** regional lymph node involvement
III	Multiple dermal tumors; large, infiltrating tumors with or without regional lymph node involvement
IV	Any tumor with distant metastasis

Prognostic Factors: Stage

I	One tumor confined to the dermis without lymph node involvement
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I	One tumor confined to the dermis without lymph node involvement
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IV	Any tumor with distant metastasis

Diagnostic Technique and Workup

1) Confirm the diagnosis
   - FNA often adequate
2) Aspirate draining lymph node
3) Bloodwork
4) Can you resect it with wide margins (1-2cm lateral, 1 facial plane deep) ?
   - Yes
     - If lymph node is negative and you can resect it → do it
     - lymph node is positive → aspirate liver and spleen (even if they appear normal)
   - No
     - Prednisone? 1mg/kg x 7-14 days (after staging)
     - Path is less clear… → call us!

- Not routine: thoracic radiographs, buffy coat smear

Diagnostic Technique and Workup

Abbreviated table 20.1
+ Lymph node
Bad location
Large Size
Breed
Fast Growth

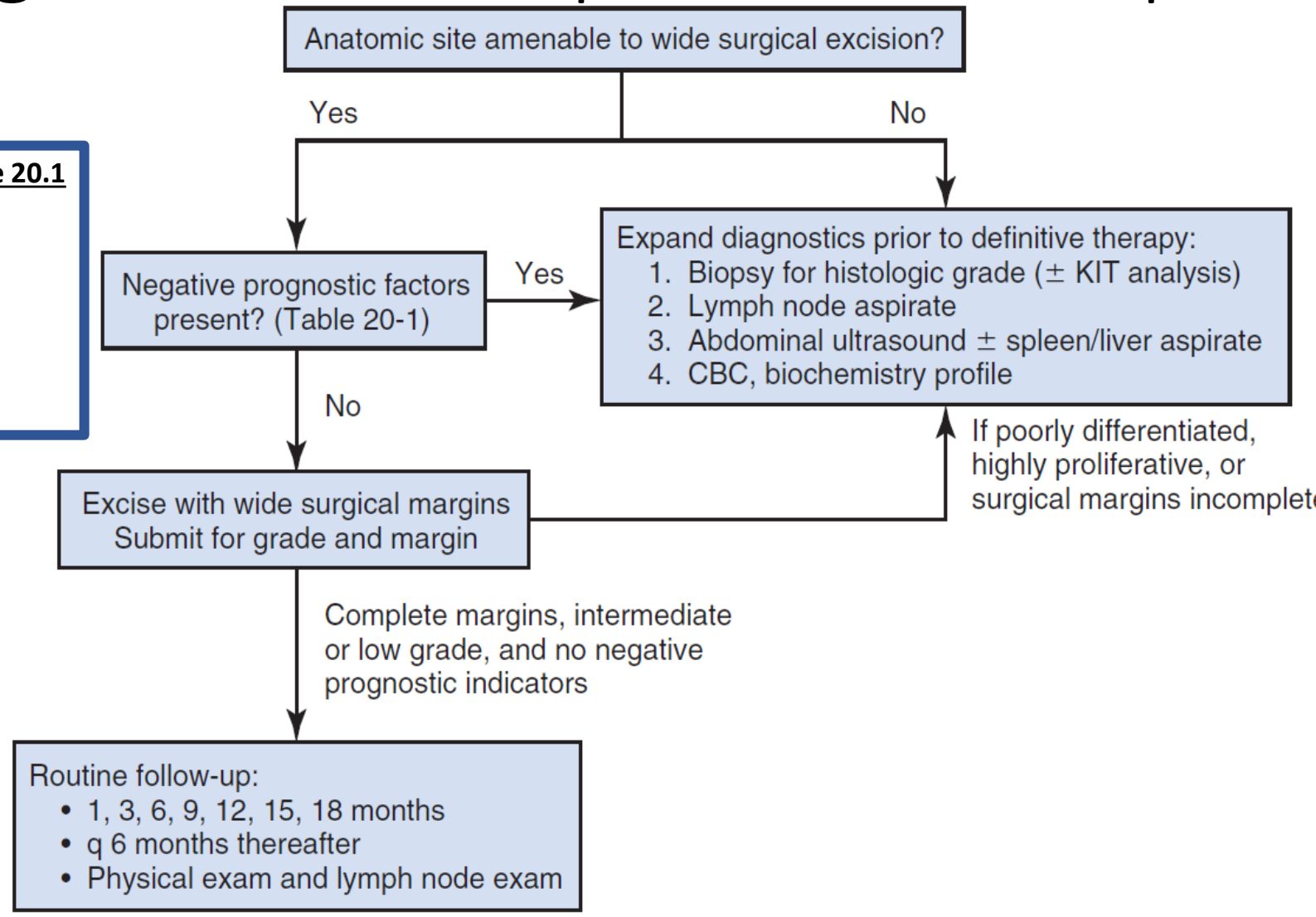


FIGURE 20-4 Suggested diagnostic steps for canine cutaneous MCTs.

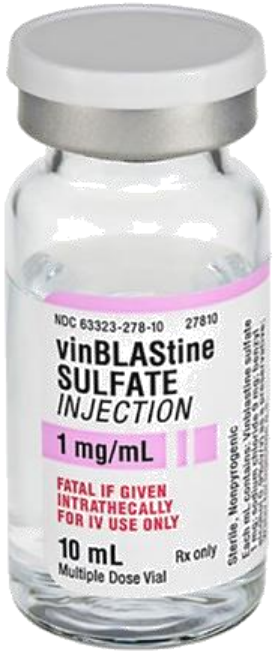
Withrow SJ. *Withrow and MacEwen's Small Animal Clinical Oncology* . 5th ed. St. Louis, MO: Elsevier

Treatment: Resectable, (-) node

- Gross margins
  - 1-2cm lateral, 1 fascial plane deep*
- Histologic margins
  - Adequate: 4mm deep (or a quality/facial plane), 10mm lateral
    - 100 dogs with low to intermediate grade tumors: no recurrence or metastasis for >2 years
    - Probably adequate: ≥3mm lateral, quality deep plane

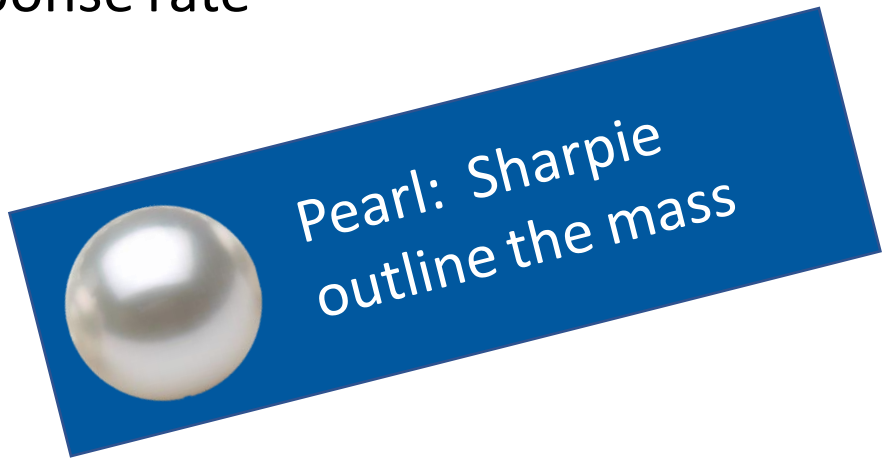
Treatment: Resectable, (+/?) node

- Intermediate to high grade by definition
- Gross/Histologic margins: same
- Take the lymph node- margin not necessary
- (+) node: Chemo is indicated AFTER resection
  - Vinblastine +/- lomustine
- Prognosis
  - Grade II stage II with chemo- good
  - Grade III stage II with chemo- poor



Treatment: Not Resectable

- Stage
- Neo-adjuvant prednisone? → now can you resect? Do it!
  - 70% objective response rate



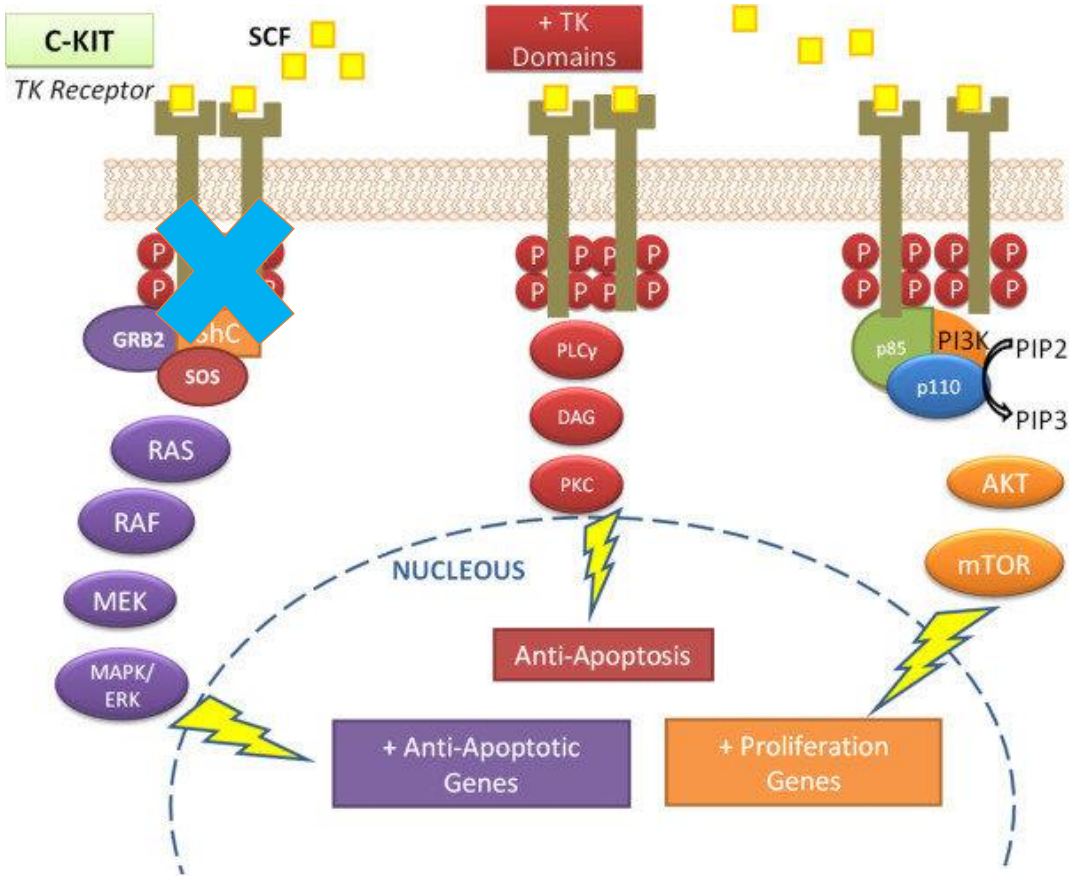
Treatment: Not Resectable

- Stage
- Neo-adjuvant not adequate
- Biopsy for grade
  - Low grade → resect
    - Incomplete
      - Active Surveillance
      - Radiation
      - Electrochemotherapy?
  - Intermediate grade
    - Is it “low” or “high” grade II- Mitotic index? Other factors?
  - High grade
    - Chemotherapy will be part of treatment → chemotherapy first? Chemotherapy alone? Oncology consult?

Treatment: Chemotherapy

- When
  - High grade OR positive lymph node after resection
  - To downstage- make a tumor resectable
  - Surgery declined

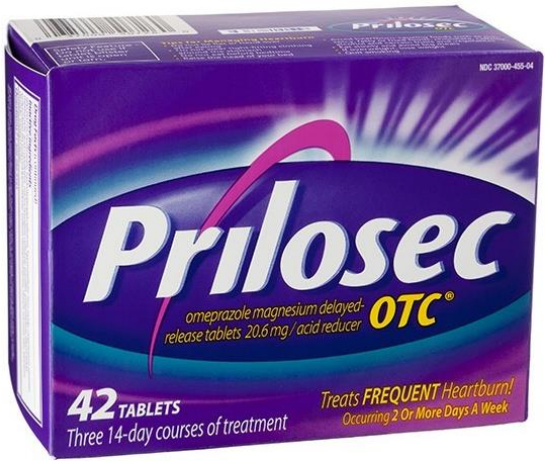
Drug	Response Rate	Notes
Vinblastine/Prednisone	47%	Longest MST for high risk MCT
Vinblastine/Pred/Lomustine	57-64%	Highest overall response rates
Lomustine	44%	economical, q3 weeks
Palladia	Ckit(+)69%, (-)37%	EOD or MWF, expensive
Chlorambucil/Pred	38%	inexpensive, good tolerability



Palladia interferes with C-Kit

Treatment: Chemotherapy

- Histamine blockade recommended in all dogs with gross disease
- Not necessary if no measurable tumor



Treatment: Multiple MCT

- Tumors are genetically unrelated
- Prognosis based on grade, stage and completeness of excision for each tumor

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Review

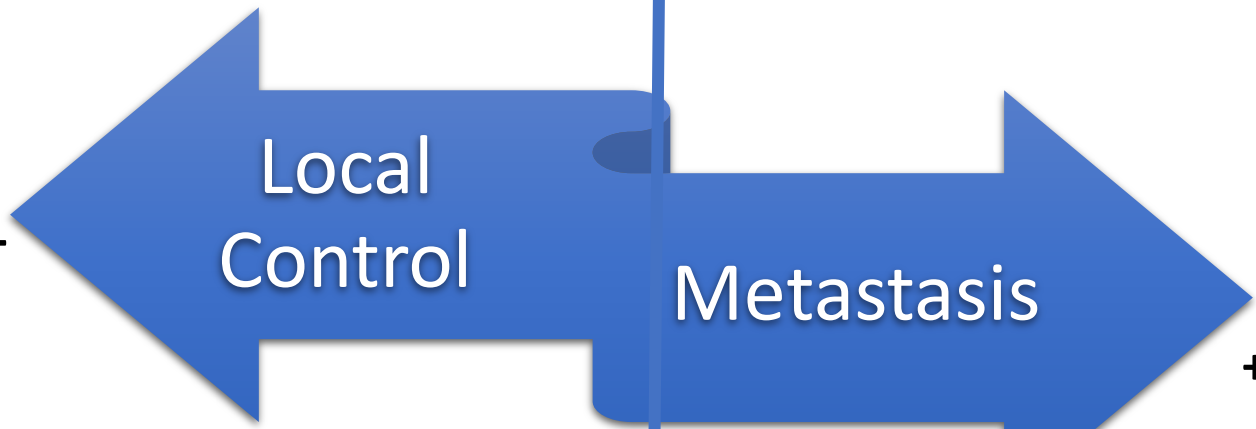
Summary

- Step 1: Confirm diagnosis
- Step 2: Stage the draining lymph node
  - If positive or tumor is clinically aggressive → full staging
  - If negative- ok to remove with wide margins
    - Neo-adjuvant prednisone?
- Step 3: Remove for grade and margins
  - Grade I
    - Can be cured with wide excision
  - Grade II
    - Mitotic index? <5 ☺
    - Ugh
  - Grade III
    - High rate of mets
    - Wide excision + chemotherapy → <1 year

Summary

- Step 4: What's the plan
  - Low grade, complete margins→ excellent prognosis
  - Low grade, dirty margins → recurrence
    - Scar revision
    - Radiation
    - Monitor: 20-30% recur (grade I, low grade II)
    - Other potentials: chemotherapy
  - High grade, complete margins → metastasis
    - Chemotherapy
  - High grade, dirty margins → recurrence and metastasis
  - Any grade with LN mets → 1) local control 2) chemotherapy
  - Visceral mets → ☹

Summary

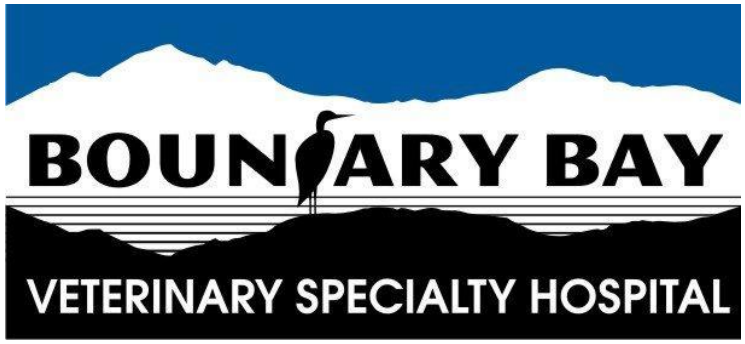


Required for all MCT

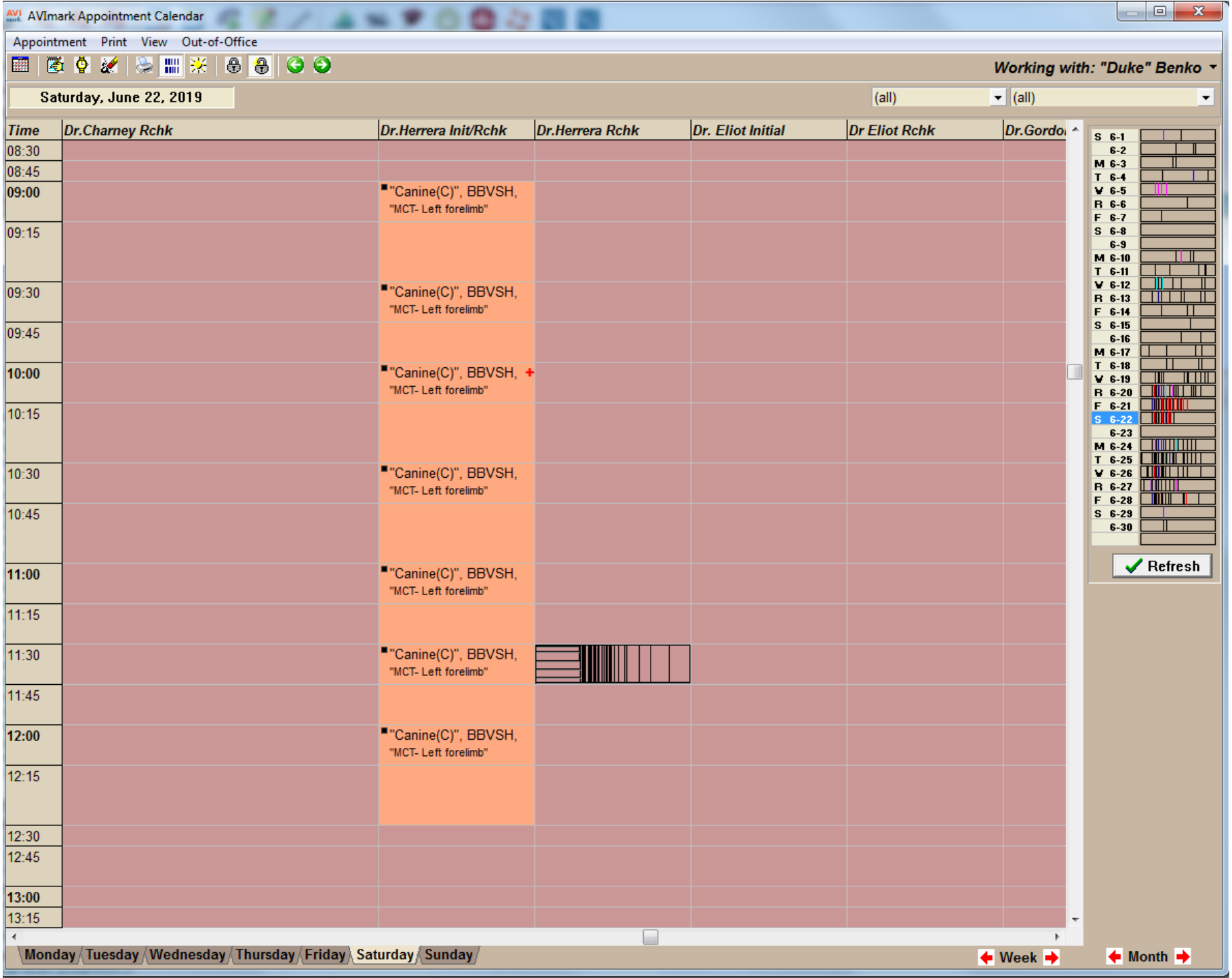
Concern for
High grade II
Grade III
+ lymph node

Approach
Wide excision
Radiation therapy
Monitor

Approach
Chemotherapy



Case Examples


AVImark Appointment Calendar
Appointment
Print
View
Out-of-Office
Working with: "Duke" Benko
Saturday, June 22, 2019
(all)
(all)
Time
Dr.Charney Rchk
Dr.Herrera Init/Rchk
Dr.Herrera Rchk
Dr. Eliot Initial
Dr Eliot Rchk
Dr.Gordo
08:30
08:45
09:00
09:15
09:30
09:45
10:00
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11:30
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13:00
13:15
"Canine(C)", BBVSH,
"MCT- Left forelimb"
S 6-1
6-2
M 6-3
T 6-4
W 6-5
R 6-6
F 6-7
S 6-8
6-9
M 6-10
T 6-11
W 6-12
R 6-13
F 6-14
S 6-15
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T 6-18
W 6-19
R 6-20
F 6-21
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R 6-27
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6-30
Refresh
Monday
Tuesday
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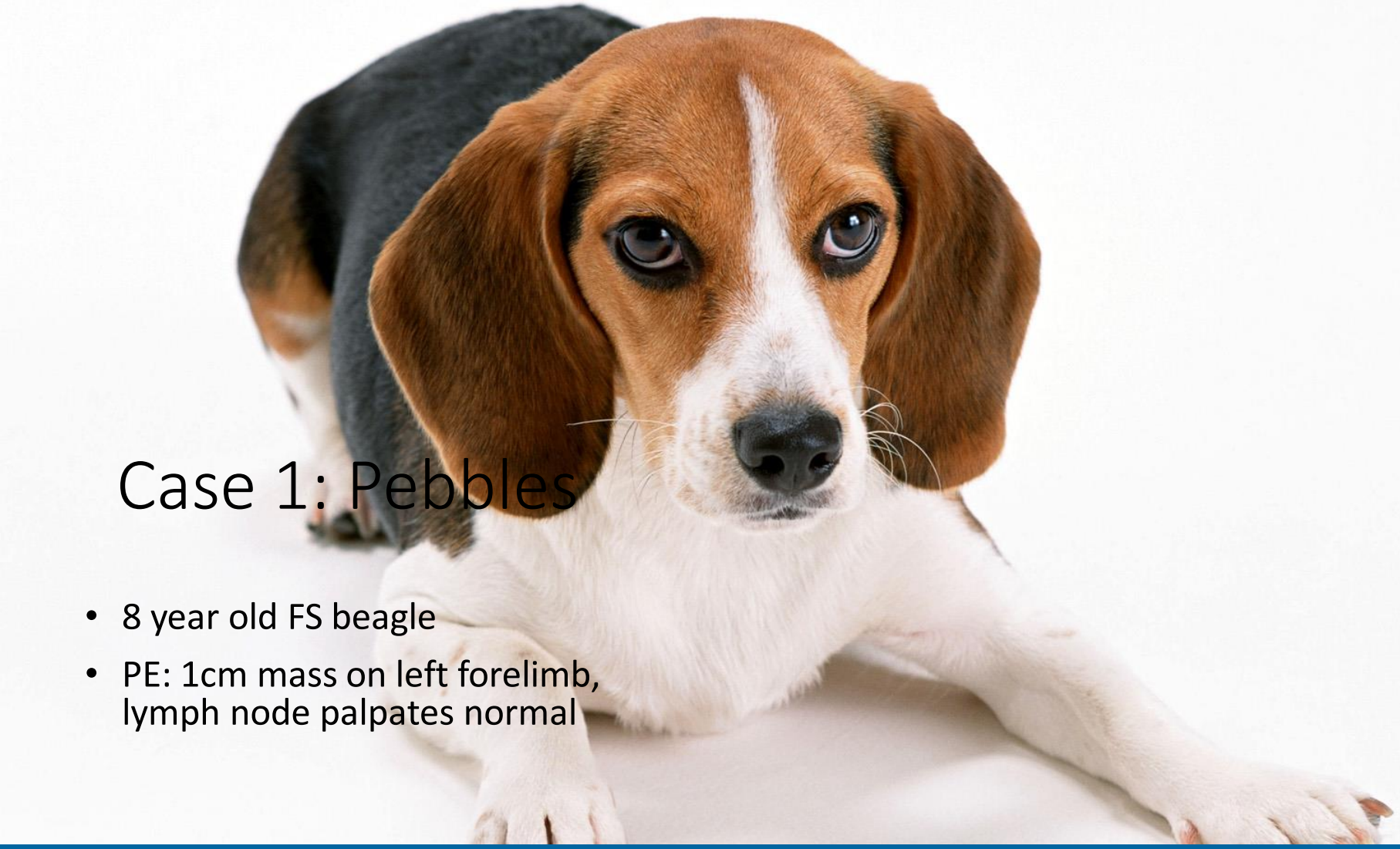
Saturday
Sunday
Week
Month



Case 1: Pebbles

- 8 year old FS beagle
- PE: 1cm mass on left forelimb, lymph node palpates normal

Case 1: Pebbles

- Step 1: Confirm
- Step 2: Any +/- prognostic factors?
  - (+): beagle, small
- Step 3: Aspirate LN
  - Negative
- Plan?
- Path Results
  - Low grade, complete excision (4mm margin)
- Prognosis

Case 2: Ginger

- Biting at a mass on left forelimb, present for 2 years
- PE: Ulcerated 2cm mass left antebrachium, LN palpates normally

Case 2: Ginger

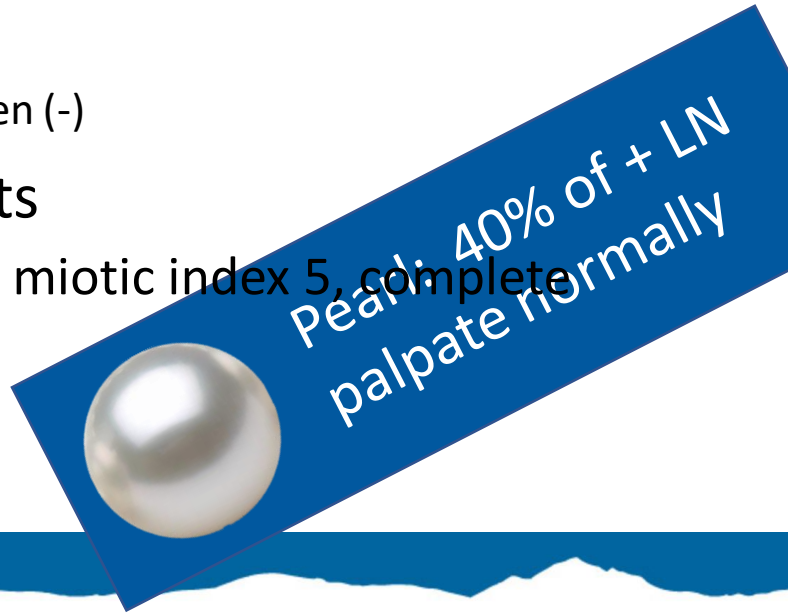
- Step 1: Confirm
- Step 2: Any +/- prognostic factors?
  - (+): Long history
  - (-): Ulcerated
- Step 3: Aspirate LN
  - Negative
- Plan?
- Path Results
  - Grade II, complete excision (2mm margin), mitotic index 3
- Prognosis

Case 3: Sammy

- 6 year old male castrated German Shepherd
- History: Mass that comes and goes
- PE: 8mm pink inflamed mass on 2nd digit of left thoracic limb, lymph node palpates normal

Case 3: Sammy

- Step 1: Confirm
- Step 2: Any +/- prognostic factors?
- Step 3: Aspirate LN
  - Positive
- Plan?
  - Liver/spleen (-)
- Path Results
  - Grade II, miotic index 5, complete excision
- Prognosis



Case 4: Sheila

- 12 year old female spayed chihuahua
- PE: Subungual mass on left thoracic limb, lymph node plump

Case 4: Sheila

- Step 1: Confirm
- Step 2: Any +/- prognostic factors?
  - (-): Subungual, plump LN
- Step 3: Aspirate LN
  - Increased mast cells, but no clusters, well differentiated → ?
- Plan?
  - Liver/spleen (-)
- Path Results
  - Grade II, mitotic index 6, complete excision
  - Lymph node +
- Prognosis

Case 5: Bongo

- 11 year old male Golden Retriever
- PE: Rapidly growing mass on left carpus, painful; enlarged left prescapular lymph node

Case 5: Bongo

- Step 1: Confirm
- Step 2: Any +/- prognostic factors?
  - (-): large, ulcerated, big LN
- Step 3: Aspirate LN
  - Positive
- Plan?
  - Liver/spleen (-)
  - Surgeon?
  - Amputate
- Path Results
  - Grade III, complete margins, + node
- Prognosis

Case 6: Shasta

- 4 year old female spayed Shar Pei
- Single mass present for several months, now rapid progression
- Low appetite, diarrhea

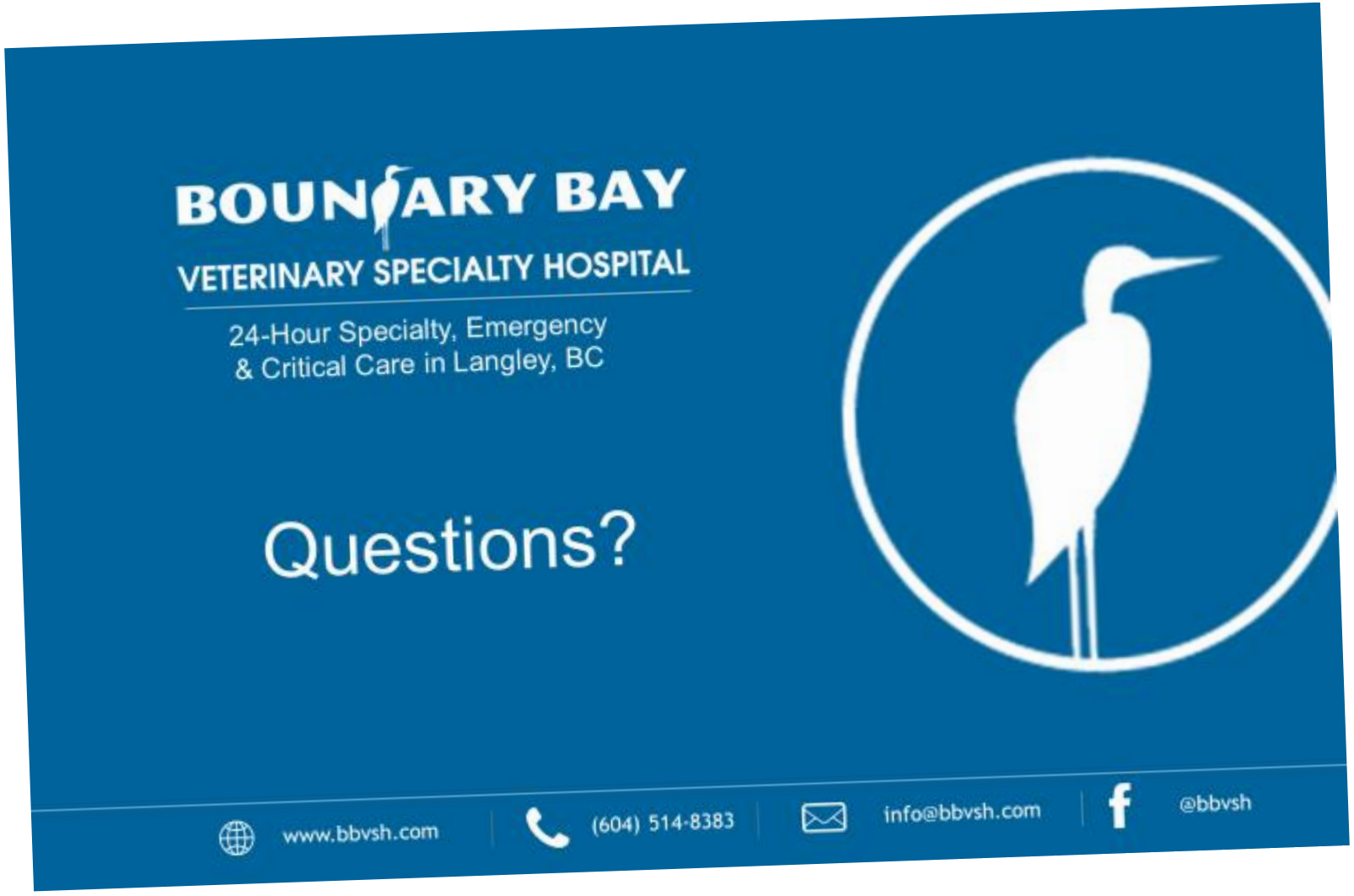
Case 6: Shasta

- Step 1: Confirm
- Step 2: Any +/- prognostic factors?
  - (-): breed, rapid growth, systemic signs concern for visceral metastasis
- Step 3: Aspirate LN
  - Positive
- Plan?
  - Liver/spleen (+)
- Prognosis

MCT in Cats

- No grading scheme
- Cutaneous: Generally need *conservative* resection
- Splenic: splenectomize, even if there is systemic involvement (MST: 1-2 year)

We are only a phone call away!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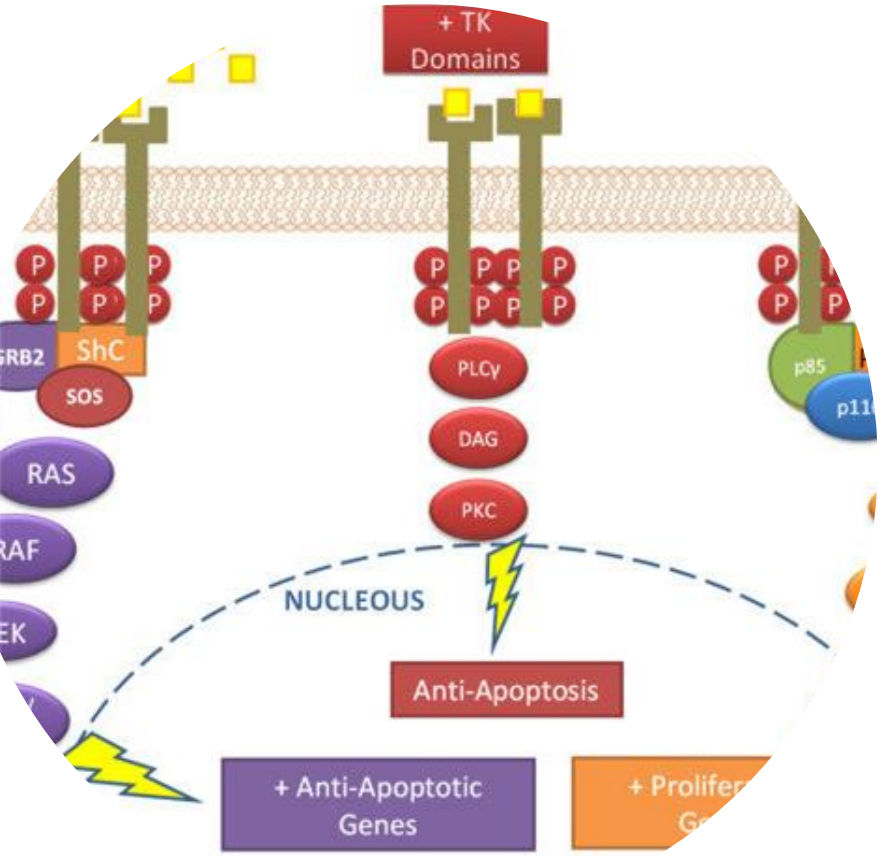
Prognostic Factors: Proliferation Markers



- Prognosis unclear? Consider prognostic panel:
  - C-kit
  - KIT staining pattern
    - aberrant expression of KIT receptor
  - PCA
  - Agnor
  - Ki67