



Welcome
We're so glad
you're here!



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Oncologic Emergencies
When Cancer Can't Wait


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Agenda


- Cancer-related emergencies
 - Life-threatening effusions
 - Respiratory distress
 - Pathologic bone fracture
 - Substage b lymphoid disease
- Emergency paraneoplastic syndromes
 - Hypercalcemia
 - Hypoglycemia
- Chemotherapy-related emergencies
 - Anaphylaxis
 - Extravasation
 - Tumor lysis syndrome
 - GI toxicity
 - Bone marrow toxicity



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Cancer-Related Emergencies


"The tumor is doing it"



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Malignant Effusions


- Effusions common, but not all are life-threatening
- Life-threatening malignant effusions:
 - Hemoabdomen – most commonly seen with hemangiosarcoma (HSA)
 - Pericardial effusion – most commonly seen with HSA
 - Significant pleural effusion – carcinomatosis, lymphoma




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Hemoabdomen

- Presentation: hypovolemic/hemorrhagic shock
 - Presenting complaints: weak, lethargic, collapse
 - PE: pale gums, thready pulses, tachycardia, fluid wave
- Diagnostic work-up:
 - PCV – peripheral vs. abdominal fluid
 - Imaging
 - Abdominal ultrasound > x-rays
 - Key organs: spleen, liver, kidney, adrenal glands, mesentery
 - Don't forget to met check with thoracic radiographs
- Immediate treatment = stabilization, transfusion, surgery



Splenic HSA, C/O M. Mason



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How Likely is Malignancy In Splenic Mass?

- Ddx – HSA, lymphoma, other sarcomas, nodular hyperplasia, hematoma
- Path studies ~50% malignant
 - 50-74% of those were HSA
- Clinical nontraumatic hemoabdomen studies
 - 63-80% had HSA
 - 2013 study - 87% due to neoplastic masses; 76% of those were HSA
 - "3/4 Rule" – ¾ malignant, ¼ of malignant are HSA
- Small dog less likely to have HSA but overall malignant:benign similar
- Larger splenic masses/heavier spleens more likely to be benign

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How Likely is Malignancy In Splenic Mass?

Benign Characteristics

- Young dog
- No hemoabdomen
- Larger mass
- Normal platelet count
- No transfusion needed

Malignant Characteristics

- Old dog
- Hemoabdomen
- Smaller mass
- Thrombocytopenia
- Transfusion needed

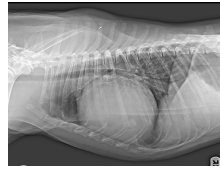
But remember, cancer does not always follow the rules!

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Pericardial Effusion

- Presentation: cardiogenic tamponade
 - Presenting complaints: lethargy, weak/collapse
 - PE: tachycardia, thready pulses, muffled heart sounds, signs of R-heart failure
- Diagnostic work-up:
 - Chest x-rays – globoid heart silhouette
 - TFAST – pericardial effusion
 - Echocardiogram to assess for mass
 - Cancer = most common cause of pericardial effusion
 - HSA most common cardiac mass; 82% of HSA cause pericardial effusion
 - Ddx – chemodectoma, lymphoma, mesothelioma
 - Cardiac troponin I
- Immediate treatment = pericardiocentesis



Clinician's Brief

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Pleural Effusion

- Presentation: respiratory distress
 - Presenting complaint: open-mouth breathing, increased respiratory effort
 - PE: quiet lung sounds ventrally
- Diagnostic work-up:
 - Chest x-rays
 - TFAST
 - Fluid cytology –challenging to interpret especially w/chronic fluid accumulations
- Immediate treatment = thoracocentesis

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Respiratory Distress

- Upper respiratory distress
 - Causes
 - Oral tumors – tonsil, larynx, pharynx
 - Cervical lymphadenopathy (i.e. lymphoma) – rare
 - Treatment – intubate, tracheostomy, surgery, L-asparaginase (lymphoma), dex-sp
- Primary pulmonary disease
 - Causes
 - Large primary lung mass (i.e. carcinoma, histiocytic sarcoma)
 - Diffuse metastasis
 - Treatment – surgery (solitary mass), chemotherapy, palliative prednisone

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Pathologic Bone Fractures

- Bone tumors
 - #1 culprit – osteosarcoma
 - MM, metastatic carcinoma
- Two treatment options:
 - Amputation (if possible)
 - Euthanasia



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Lymphoid Neoplasia

- Dogs with lymphoma or leukemia can decline quickly
- Substage matters
 - Substage a = feeling well at diagnosis
 - Substage b = feeling sick at diagnosis
 - Signs usually vague – lethargy, anorexia, GI upset, fever
- Substage b cases should be seen on urgent basis (i.e. within 24-48 hours)
 - If referral not option:
 - Obtain minimum diagnostics: CBC, chemistry panel, lymph node aspirate
 - Send cytology for pathology review! If not, at least save or send with owner for referral
 - Start steroids: prednisone 2mg/kg SID x 7 days, 1.5mg/kg SID x 7 days, 1mg/kg SID indefinitely
 - Chemotherapy ideally should be started within 7-10 days of starting prednisone!
- Supportive medications PRN

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Emergency paraneoplastic syndromes

"The tumor is doing it, but indirectly"

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Paraneoplastic Syndromes (PNS)

- PNS: alteration in structure or function that occurs distant to tumor
 - Diverse clinical abnormalities
 - Associated with non-invasive actions by tumors
 - Can be 1st sign of malignancy
 - Can be hallmark of certain tumor types
 - Often parallel to their corresponding tumor
 - CAN BE EMERGENCIES
 - Hypercalcemia
 - Hypoglycemia

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Hypercalcemia

- **G** – Granulomatous disease
 - **O** – Osteolysis
 - **S** – Spurious
 - **H** – Hyperparathyroidism (primary)
- Cancer is
#1 cause in dogs,
#3 cause in cats
- **D** – Vitamin D toxicity
 - **A** – Addison's
 - **R** – Renal (secondary hyperparathyroidism)
 - **N** – Neoplasia ("Hypercalcemia of Malignancy = HM")
- **I** – Idiopathic
 - **T** – Temperature (hypothermia)

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Hypercalcemia - Clinical Signs

- Lethargy
 - CNS depression
 - Weakness, shaking / twitching
 - Bradycardia +/- arrhythmia
- Gastrointestinal
 - Vomiting
 - Anorexia
 - Decreased GI motility
- Renal impairment and azotemia
 - Decreased renal blood flow and GFR
 - Renal calcification and tubulointerstitial inflammation
 - PU / PD --> dehydration



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Cancers that Cause Hypercalcemia

- T-Cell Lymphoma
- Anal sac apocrine gland adenocarcinoma (AGASACA)
- Thyroid carcinoma
- Multiple myeloma (MM)
- Bone tumors
- Thymoma
- Squamous cell carcinoma
- Mammary gland carcinoma/adenocarcinoma
- Melanoma
- Primary lung tumors
- Chronic lymphocytic leukemia
- Parathyroid gland tumors

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Hypercalcemia Work-Up

- Thorough physical examination
 - Peripheral lymph nodes
 - If large – obtain cytology +/- flow cytometry BEFORE STEROIDS
 - Digital rectal examination to rule in/out anal sac mass
 - Cervical palpation
- Blood work
 - CBC – look for lymphocytosis, seen with lymphoma or MM
 - Chemistry panel –renal values, hyperglobulinemia (MM)
 - Any patient you suspect has lymphoma or anal sac tumor
 - Urinalysis
 - Malignancy Profile at MSU
- Imaging
 - Chest x-rays –mediastinal mass, pulmonary metastasis
 - Abdominal ultrasound – enlarged lymph nodes, liver/spleen changes

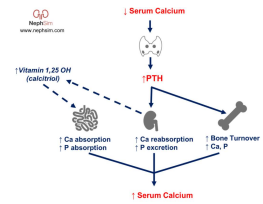
Test Name	Result	Reference Range
Complete Blood Count (CBC)	WBC: 12,000	5,000 - 15,000
Chemistry Panel	BUN: 15	7 - 20
Urinalysis	SGOT: 10	0 - 20
Malignancy Profile	MM: 1.5	< 1.0
	ALP: 100	0 - 100
	Ca: 15	9 - 12
	P: 4	2.5 - 4.5

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MOA of Hypercalcemia of Malignancy

- Most common is excessive production of PTH-rP
 - Lymphoma, AGASACA
- Ectopic production of PTH
- Extensive lytic bone tumors – i.e. widespread carcinoma metastasis
 - Mammary, lung, prostate, liver
 - Rarely primary bone tumors
- Tumor-associated cytokine release
 - Prostaglandins, interleukins, etc



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Treatment of Hypercalcemia

- Immediately = protect kidneys!
 - 0.9% NaCl preferred; promotes calciuresis via increased GFR
- Steroids – decrease calcium via decrease bone and GI calcium resorption and increased renal excretion
 - Can interfere with diagnosing lymphoma – obtain samples first
- Bisphosphonates– inhibit osteoclastic bone resorption
- Treat underlying cancer quickly
 - Lymphoma → L-asparaginase, chemotherapy
 - Anal sac adenocarcinoma → surgery, radiation, chemotherapy



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Hypoglycemia

- Blood glucose < 60 – 70 mg/dL
 - Hypoadrenocorticism
 - Starvation
 - Over-exertion ("Hunting dog hypoglycemia")
 - Sepsis
 - Liver dysfunction
 - Laboratory error or spurious
 - Severe hemococoncentration / Polycythemia can affect glucometer reading!!!!
 - Neoplasia



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Hypoglycemia – Clinical Signs

- Weakness or disorientation
- Ataxia
- Collapse
- Seizures
- Behavior changes
- Muscle tremors
- Anxiety

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Cancers that Cause Hypoglycemia

- Insulinoma / Beta cell pancreatic tumor
- Leiomyosarcoma
- Hepatocellular carcinoma
- Plasma cell tumor
- Lymphoma
- Mammary tumor
- Adenocarcinoma
- Hemangiosarcoma

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Work-up of Hypoglycemia

- Thorough physical examination
- Minimum data base:
 - CBC
 - Chemistry panel
 - Urinalysis
- Submit insulin glucose ratio
 - Elevation usually noted with insulinoma, but can be high with other tumors
- Imaging
 - Chest x-rays
 - Abdominal ultrasound – detects <50%
 - CT scan – better
- Exploratory laparotomy – most tumors visible or palpable

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MOA of Hypoglycemia of Malignancy

- Insulinoma
 - Secrete insulin
 - Increased tumor utilization of glucose
 - Decreased hepatic glycogenolysis
 - Insulin-like growth factors
- Other tumors = other hormones
 - Glucagon, Somatostatin, Pancreatic polypeptide
 - Growth hormone, IGF-1, Gastrin

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Treatment of Hypoglycemia

- Immediately = Dextrose bolus or CRI; glucagon CRI
- Diet – small, frequent meals
 - High fat, high protein, complex carbs
- Control hypoglycemia
 - Prednisone
 - Starting dose 0.25mg/kg BID, increase PRN
 - Diazoxide
 - Octreotide
- Chemotherapy
 - Streptozotocin
 - Palladia
- Surgery – even if no mass found on imaging; take as much disease as you can



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Chemotherapy-Induced Emergencies

"The treatment did it"

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Timing of Side Effects

Immediate (up to 48 hours)	Delayed Acute (days – weeks)	Cumulative/Chronic (weeks to months)
<ul style="list-style-type: none"> • Anaphylaxis <ul style="list-style-type: none"> • Doxorubicin • L-asparaginase • Extravasations <ul style="list-style-type: none"> • Doxorubicin • Vincristine • Vinblastine • Tanovea • Mustargen • Tumor lysis syndrome 	<ul style="list-style-type: none"> • GI upset (days 1-5) • Bone marrow suppression (days 6-21) 	<ul style="list-style-type: none"> • Cardiotoxicity (dog) <ul style="list-style-type: none"> • Doxorubicin • Hepatotoxicity <ul style="list-style-type: none"> • CCNU (lomustine) • Renal toxicity <ul style="list-style-type: none"> • Doxorubicin (cat) • CCNU (cat) • Carboplatin (dog, cat) • GI ileus <ul style="list-style-type: none"> • Vincristine

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Anaphylaxis

- Culprits:
 - L-asparaginase –foreign protein (derived from *E.coli*)
 - Doxorubicin – stimulates histamine release
- Clinical signs vary by species:
 - Dogs: Skin and GI
 - Cats: Lungs and GI
- Immediate treatment
 - STOP chemotherapy administration
 - Antihistamine, steroids, IV fluids to combat vasodilatory shock
 - Severe cases – epinephrine

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Extravasation

- Main culprits:
 - Doxorubicin
 - Vinca alkaloids
 - Tanovea
 - Mustargen
 - Bisphosphonates
- MOA – tissue damage d/t free radical formation
- Tissue necrosis 1-10 days after injection
 - Range from erythema to open wounds

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Extravasation Treatment

Treatment Goal: Localize and Neutralize		Treatment Goal: Disperse and Dilute	Treatment Goal: Monitor for Mild Inflammation
Vesicants	Irritants	Vesicants	Non-Irritants
Dactinomycin* Carboplatin*		Vinclosterin†	L-Asparaginase
Doxorubicin* Doxorubicin‡	Cisplatin*	Vincristine§	Bleomycin
Mitomycin* Mitomycin‡	Dacarbazine*	Vinorelbine*	Cyclophosphamide
Misoprostol* Flutamide*	Fluorouracil¶		Cytarabine
Paclitaxel** Melphalan*			Gemcitabine
			Methotrexate

1. Localize
 Apply dry cold compresses for 30–30 min at a time, 4 times a day for the first 24–48 hr following extravasation.

2. Neutralize
 Use the antidote specific to the agent.

1. Disperse
 Apply dry warm compresses for 20–30 min at a time, 4 times a day for the first 24–48 hr following extravasation.

2. Dilute
 Use the antidote specific to the agent.

Apply dry/cold compresses for about 20–30 min, then as needed.

AAHA

*No recommended antidote. †Recommended antidote: dexrazoxane or dimethyl sulfoxide (DMSO). ‡Recommended antidote: DMSO. §Recommended antidote: hyaluronidase. Adapted from [1].

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Tumor Lysis Syndrome

- Rare in dogs, more common in people
- Most commonly occurs with high-grade/high-stage lymphoma/leukemia
 - High tumor burden, dehydrated, underlying kidney disease = higher risk
 - Rapid response to therapy (chemo or RT) = higher risk
 - Dogs > cats
- Rapid lysis of tumor cells after initiation of therapy leads to:
 - Hyperphosphatemia
 - Hyperkalemia
 - Hypocalcemia
 - Metabolic acidosis +/- azotemia
- Presentation – severe lethargy, GI signs, cardiovascular collapse/shock
- Treatment – aggressive fluid diuresis, correction of electrolyte/acid-base imbalances

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Who is at Risk for GI/BM Toxicity?

- Breed sensitivities – mutant MDR1 gene
 - MDR1 gene encodes P-glycoprotein – drug transport pump involved in drug *absorption, distribution and excretion*
 - Dogs with mutation = more susceptible to severe drug toxicity
- Drugs:
 - Acepromazine
 - Butorphanol
 - Doxorubicin
 - Erythromycin
 - Ivermectin
 - Loperamide
 - Milbemycin
 - Moxidectin
 - Paclitaxel
 - Sefamandol
 - Vinorelbine
 - Vincristine
 - Vinorelbine

Breed	Frequency
Collie	70%
Australian Shepherd (incl. Mini)	50%
Long-haired Whippet	50%
Silken Windhound	30%
McNab	30%
Chinook	25%
Shetland Sheepdog	15%
English Shepherd	15%
German Shepherd	10%
Herding Breed Cross	10%
Mixed Breed	5%

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GI Side Effects - MOA

- Vomiting/Nausea
 - Activation of the chemoreceptor trigger zone (CRTZ)
- Diarrhea
 - Apoptosis of rapidly dividing epithelial cells in GI tract
 - Upregulation of pro-inflammatory cytokines
 - Increase intestinal permeability
 - Changes in gut microbiota
- Inappetence and cachexia
 - Enhanced inflammatory cytokine responses

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GI Side Effects - Treatment

- Rarely life-threatening
- Consider future 5-20% dose reduction (based on severity of s/e)
- Treatment – what I do:
 - Anti-nausea: Cerenia, ondansetron*, metoclopramide, Pepcid/Prilosec
 - Anti-vomiting: Cerenia, ondansetron*, Pepcid/Prilosec
 - Anti-diarrhea: metronidazole, tylosin, loperamide**, probiotics
 - Inappetence: Entyce, Cerenia, mirtazapine, cyproheptadine

*Goodrx.com coupons for ondansetron save \$

**Loperamide = MDR1 substrate, careful in at risk breeds

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Types of Myelosuppression

- Neutropenia, thrombocytopenia, anemia
- Rate of disappearance of individual blood cell lines correlates with life span:
 - RBC — 120 days (dogs), 70 days (cats)
 - Platelets — 5 days to 10 days
 - Neutrophils — 4 to 10 hours
- What does this mean clinically?
 - See neutropenia 1st
 - Followed by thrombocytopenia
 - Anemia = rare, usually only mild to moderate
 - Eosinopenia, lymphopenia, monocytopenia – not typically significant

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Chemotherapy-induced Neutropenia

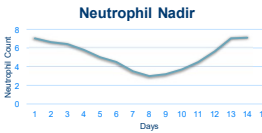
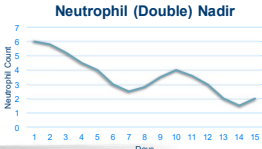
- **Most life-threatening cytopenia associated with chemotherapy!!**
- MOA – chemotherapy kills rapidly dividing cells
 - Target – cancer
 - “Innocent bystanders” – cells of GI tract, bone marrow
- Drugs vary in myelosuppressive properties
- Sequela of neutropenia:
 - Blunts inflammatory response → bacterial multiplication → life-threatening infections
 - Blunts signs and symptoms of infections
 - Chemotherapy dose reductions and delays → possibly affects outcome

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Neutropenia - Timing

- ▶ Neutrophil nadirs typically 6-10 days after tx
 - ▶ Routinely check CBC 7 days post-chemo
 - ▶ Counts rebound from nadir in 2-4 days
- ▶ Exceptions:
 - ▶ Carboplatin – delayed or double nadir
 - ▶ Check CBC at 7 days and 14 days
 - ▶ Lomustine (CCNU), esp in cats
 - ▶ Check CBC weekly after first dose

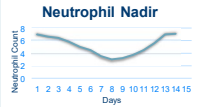



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Neutropenia - Treatment

GRADE	# NEUTS	TREATMENT
I	1500 - Low end RR	None
II	1000-1499 (1.0-1.49)	None
III	500-999 (0.5-0.99)	No fever – oral antibiotics* Fever – hospitalize and IV antibiotics**
IV	< 500 (<0.5)	GCSF?



Cut-off for antibiotics = <1000 neutrophils

*Oral antibiotics = 5-7 days of broad spectrum (Clavamox, TMS)
**IV antibiotics = Unasyn AND Baytril; discharge on oral antibiotics as soon as normothermic

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Neutropenia - Treatment

- If sending oral antibiotics home:
 - Teach owners to monitor for lethargy and fever
 - Encourage minimal exposure to pets outside home
 - Aka no doggy day care, dog parks for ~5-7 days
- If hospitalizing:
 - Try to minimize time in hospital (when afebrile, send home)
 - Keep in low-traffic area of hospital away from infectious disease patients
 - Wear gloves when handling patient as well as their blood and excrement
 - Cage signs recommended for staff
 - Wipe ports with alcohol prior to use

CHEMO
Wear Gloves
When Handling

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GCSF (Neupogen or Filgrastim)

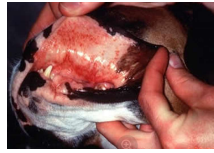
- GCSF = hematopoietic growth factor
 - Promotes proliferation and maturation of neutrophil precursors in BM → increases neutrophil count
- In people
 - Reduces duration of grade 3/4 neutropenias, febrile neutropenias, +/- hospitalization time
 - Well tolerated, most common S/E = bone pain
 - Use controversial; unclear if there is a reduction in mortality, unlikely to be cost effective
 - Only use for extremely high-risk chemotherapy protocols
- In veterinary medicine
 - Canine recombinant GCSF is not readily available and is extremely \$\$
 - Human alternatives \$\$ and risk of cross-species antibody production

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Chemotherapy-induced Thrombocytopenia

- Rarely life-threatening
 - Confirm # with manual count
- MOA – depends on drug; may:
 - Reduce platelet production (kill rapidly dividing cells)
 - Stem cells
 - Megakaryocytes
 - Platelet release from megakaryocytes
 - Increase platelet destruction
- Sequela of thrombocytopenia:
 - Bleeding risk:
 - <50,000 at risk for spontaneous bleed
 - Results in chemotherapy dose reductions and delays → possibly affects outcome



Merck Veterinary Manual

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Thrombocytopenia - Treatment

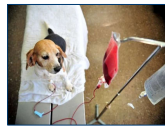
I	100K – Low end RR	Usually none
II	50 – 99k	Warn owners about bleeding risk
III	25 – 49k	Teach owners to monitor for petechia, ecchymoses, epistaxis
IV	< 25 k	If clinical/bleeding - consider transfusion – FWB, PRP, PC

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Chemotherapy-induced Anemia

- Rarely life-threatening
- Anemia very likely to be multifactorial:
 - Could it be the cancer?
 - Hemangiosarcoma, leukemia or stage V lymphoma, hemophagocytic histiocytic sarcoma, mast cell tumor, many
 - Could it be something else?
 - Anemia of chronic disease, IMHA, renal dysfunction, etc
- Treatment: address other causes, blood transfusion if clinical



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