# Mastocytosis!

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@bloodman

OHSU GENERAL HEMATOLOGY

# DISCLOSURE

**Current Relevant Financial Relationship(s)**

**None**

# Outline of Talk

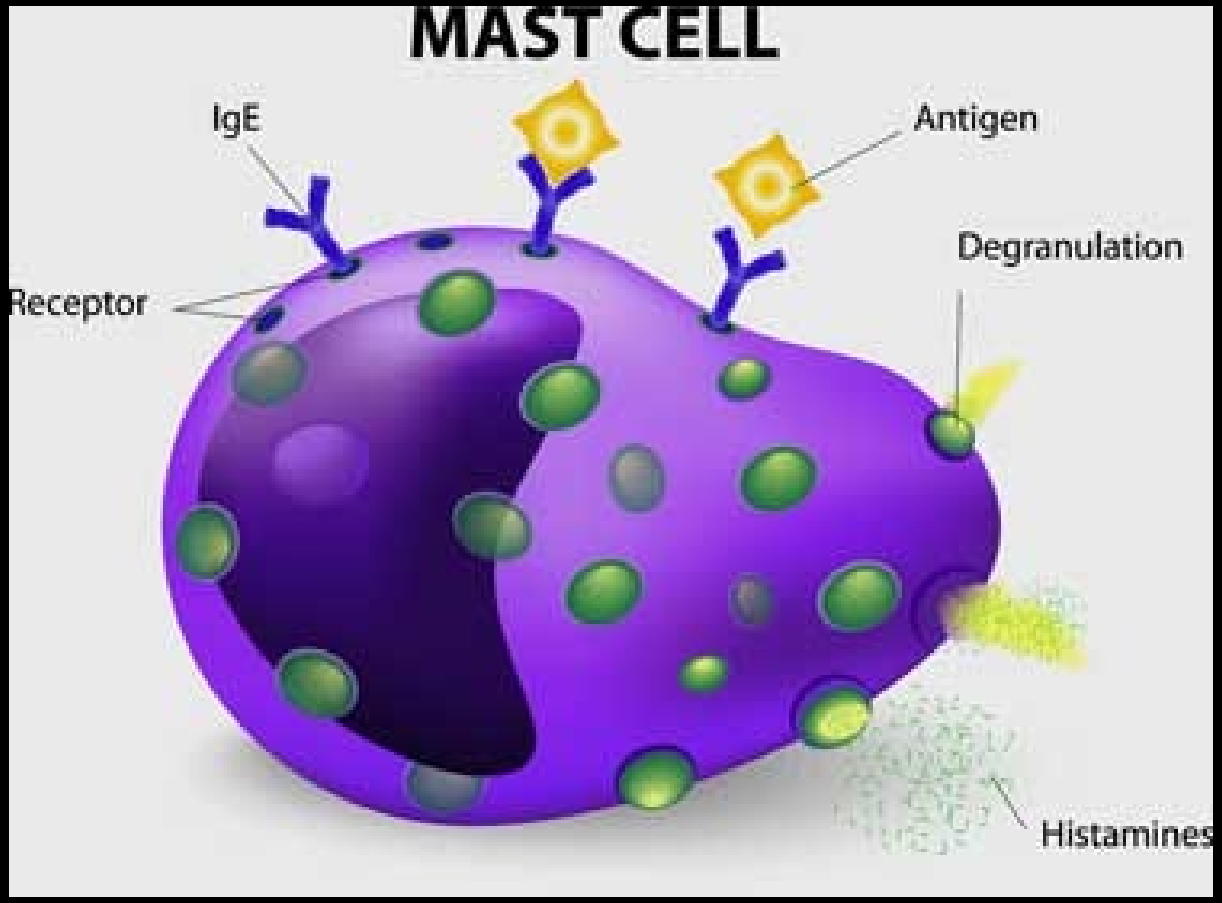
- Mast Cells
- Mastocytosis
  - Types
  - Diagnosis
  - Therapy

# Mast Cell Normal Function

- Found in normal tissues esp skin, lungs, and GI track
- Normal function to aid in inflammation
- Can selectively release granules or all at once
- Contains and creates chemical mediators (> 200)
- Lead to symptoms: flushing, urticaria, itching, wheezing etc.

# Mast Cell Mediators

- Histamine: wheezing, flushing, itching, angioedema
- Prostaglandins: wheezing, diarrhea, cramping, abdomen pain, hypotension
- Serotonin: flushing, diarrhea


MAST CELL
IgE
Antigen
Degranulation
Receptor
Histamines

# Mastocytosis

- Etiology due to overactive or too numerous mast cells
- Incidence ~10/10,000
- Under recognized

# Types of Mastocytosis

- "Mast Cell Activation Syndrome"
- Cutaneous Mastocytosis
- Indolent systemic Mastocytosis
- Smoldering Mastocytosis
- Aggressive Mastocytosis
- Mastocytosis with hematological malignancy
- Mast cell leukemia

# Mast Cell Activation Syndrome

- Not clonal
- Strict Diagnostic criteria
  1. Symptoms in two or more organ systems
  2. Markers of mast cell activation present (high tryptase etc..)
  3. Responds to mast cell therapy

# Cutaneous Mastocytosis

- Most often in children and resolves by adulthood
- Systemic issues rare
- Adults can have cutaneous signs as part of more systemic disease

# Indolent Systemic Mastocytosis

- Most common
  - ~50% of patients
- Clonal
- Issues revolve around excessive mast cell activation

# Indolent Systemic Mastocytosis

- Symptoms
  - Mast cell release symptoms
  - Gastrointestinal especially
- No impact on survival
- Rare conversion to more aggressive mastocytosis (~1%)
- Symptoms control biggest issue
  - 70% functional limitation

# Indolent Subtypes

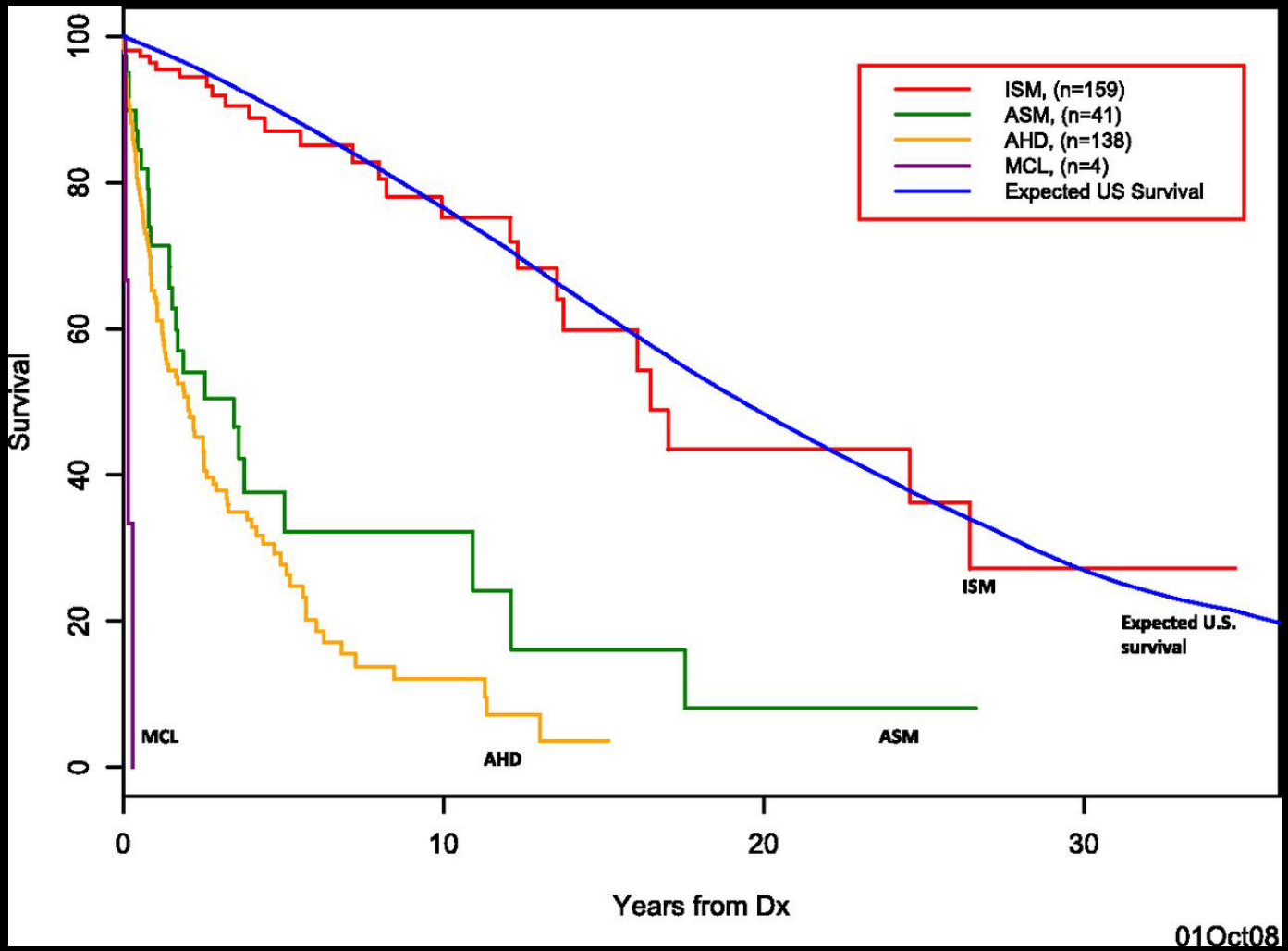
- Bone marrow MC
  - Mast cells only in marrow
  - Can have mast cell release symptoms
  - Sometimes asymptomatic
- Smoldering

# Smoldering Mastocytosis

- Diagnosis
  - > 30% marrow involvement
  - Hepatomegaly
- Inferior survival
- Higher rate of progression (18%)

# Aggressive Mastocytosis

- End organ damage
- Less mast cell activation symptoms – more “cancer”
- Tryptase > 200 ng/ml
- Poor survival


ISM, (n=159)
ASM, (n=41)
AHD, (n=138)
MCL, (n=4)
Expected US Survival
Survival
100
80
60
40
20
0
0
10
20
30
Years from Dx
ISM
Expected U.S. survival
ASM
AHD
MCL
01Oct08

# When Should You Suspect Mastocytosis?

- Anaphylaxis
- Mast cell release symptoms
- Skin disease
- GI symptoms
- Osteoporosis

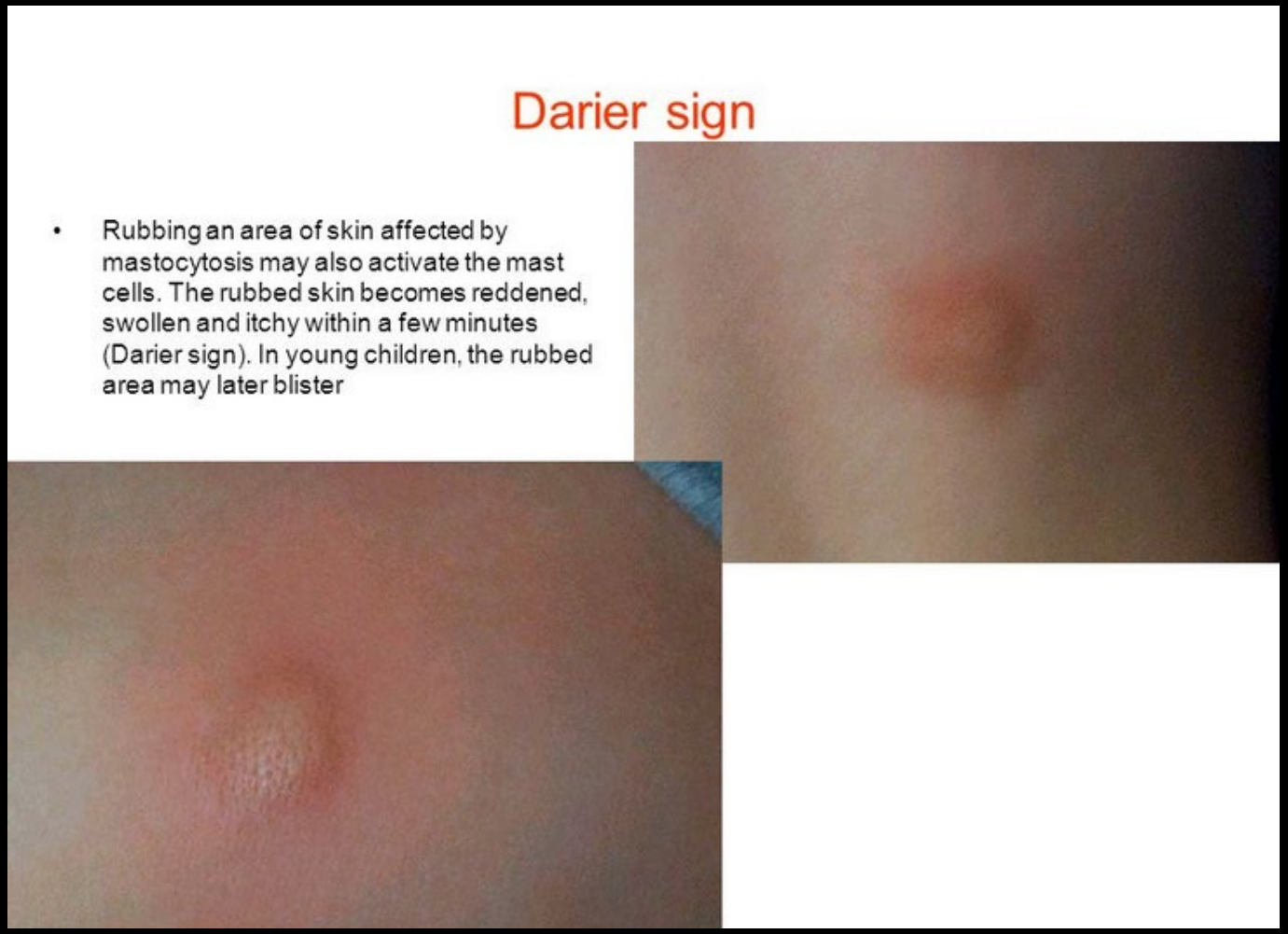
# Anaphylaxis

- Idiopathic
  - Especially recurrent
- Stings (most common)
  - 12% of anaphylaxis due to bee stings have mastocytosis
- Higher tryptase = higher risk
- IgE levels lower
  - Can lead to false negative testing

# Skin

- Itching
- Urticaria not predominant
- Dermatographism
- Darier sign

# Darier Sign

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# Gastrointestinal

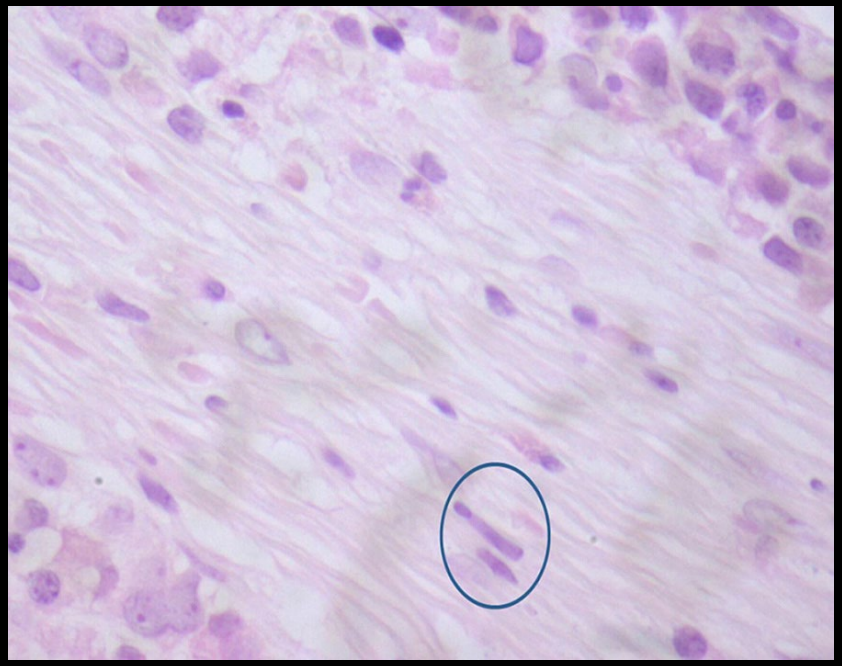
- Very common
- Often major issue
- N/V/D
- Peptic ulcers
- Abdominal pain

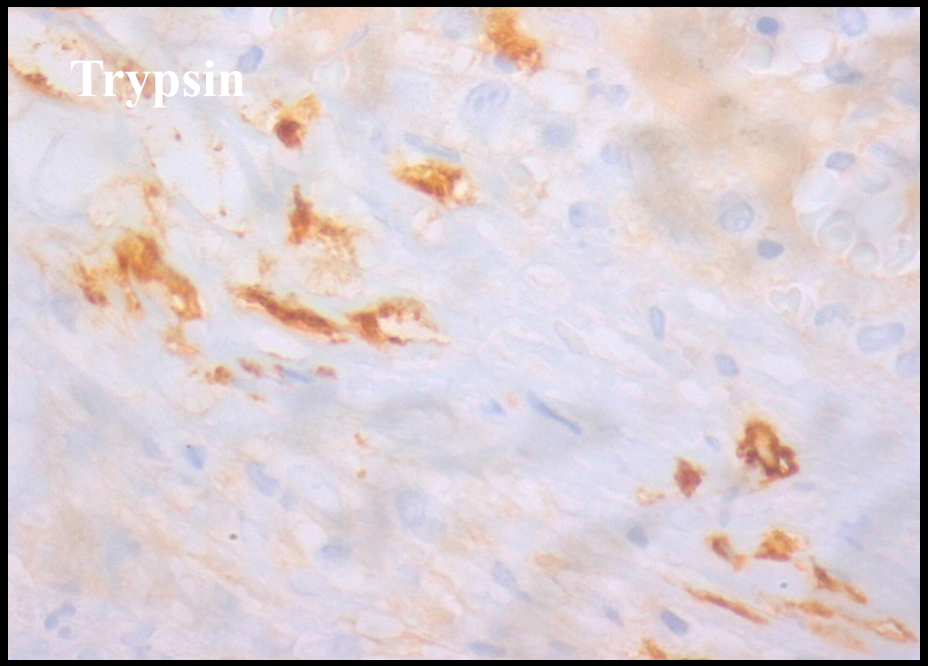
# Diagnosis

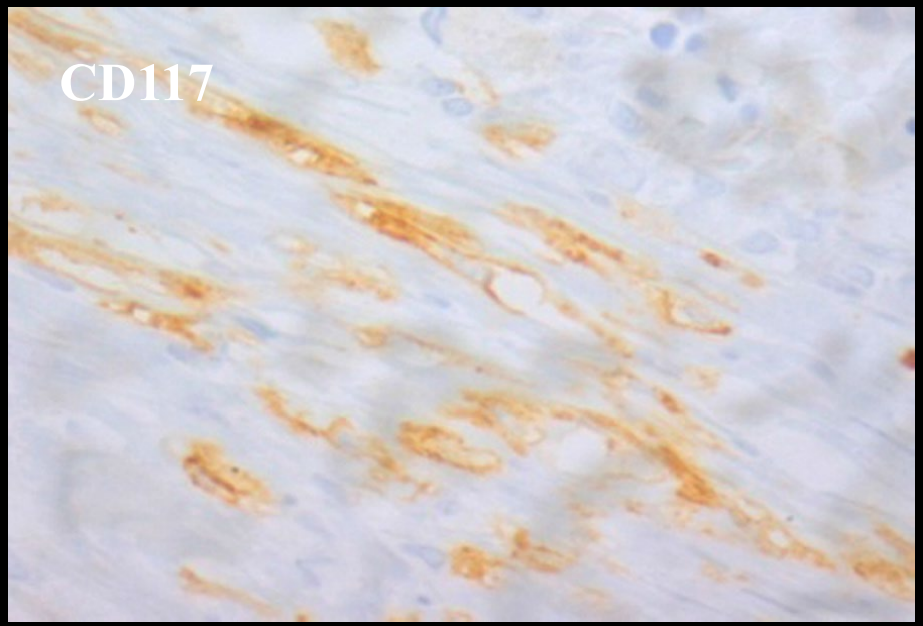
- Major: aggregates of > 15 mast cells in a non-skin biopsy
- Minor:
  - Abnormal mast cell morphology
  - Abnormal proteins on mast cell surface
  - D816V KIT mutations
  - Tryptase > 20ng/ml

# Laboratory

- Tryptase most specific
- 24-hour urine for PGD2
- Blood for c-KIT mutation
- Biopsy
  - Consider bone marrow, GI, or skin biopsy
  - May need special stains – alert pathologist to diagnosis



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# Tryptase

- Can be elevated with acute anaphylaxis
- Opioids can elevate
- > 20 ng/ml criteria
- Persistently high also worrisome

# C-KIT Mutation

- Growth factor receptor
- Key mutation in mastocytosis
- > 90% have D816V mutation
  - Rest in other areas of C-KIT
- Key test for mastocytosis

# C-KIT

- Marrow testing use to be recommended
- Now can test on peripheral blood
- Low suspicion – negative test rules out
- Positive test – helps diagnosis

# Evaluation

- Blood for c-KIT
- Biopsy of suspicious areas
- Serum tryptase
- Bone marrow for staging and equivocal cases

# General

- Symptom trigger avoidance
- Therapy of mast cell mediator release
- Treatment of bone disease
- Cytoreduction

# Hereditary Alpha Tryptasemia

- Extra tryptase gene leads to higher serum tryptases
- Some patients with increased mast cells and symptoms
- Proprietary genetic test
- DX: high tryptase negative work-up
- RX: like indolent mastocytosis

# Epi-Pens

- Anaphylaxis common
- Mastocytosis kits
  - Epi-pens
  - Antihistamines
  - Steroids

# Antihistamines

- Antihistamines (sometimes need high dose)
  - Diphenhydramine toxicity can be an issue
- Cyproheptadine
  - Also blocks serotonin
  - Diarrhea, flushing, headaches
- Doxepin
  - itching

# Dosing

- Can dose escalate
  - Cetirizine 10mg qid
  - Fexofenadine 180mg bid
  - Hydroxyzine 25mg  qid
- Non sedating during day and sedating at night
- Allergy/Immunology can help!

# H2 blockers

- Helps with GI symptoms
  - Cramping, nausea, vomiting
- May help with other symptoms
- Sometimes adding PPI can help

# Cromolyn

- Mast cell stabilizer
  - GI, skin, neuropsychiatric
- Dose: 1-200mg qid
- Can see GI symptoms
  - May need to start low and build up

# Bisphosphonates

- Bone pain and osteoporosis major issues
- Oral or IV
- Vitamin D should be checked
- All patients need bone densitometry

# Steroids

- May help with flares
- Many long term issues