# Bone Marrow Biopsy is Indicated in Idiopathic Anaphylaxis

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# Con- Part 1

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# Idiopathic Anaphylaxis vs. Mast Cell Activation Syndrome : A Bone Marrow Biopsy is *Indicated*
## Objectives

- Review indications for bone marrow biopsy in patients with anaphylaxis (severe hypotension, Hymenoptera sting reactions, recurrent episodes without trigger)
- Review the data on frequency of patients presenting with anaphylaxis and elevated tryptase who have MMCAS or mastocytosis
- Refute the case that a bone marrow biopsy is *always* indicated for idiopathic anaphylaxis

## TABLE E1. Frequency of occurrence of signs and symptoms of anaphylaxis (JACI 2010;126:480.e35)

- Dizziness, syncope, hypotension 30-35%

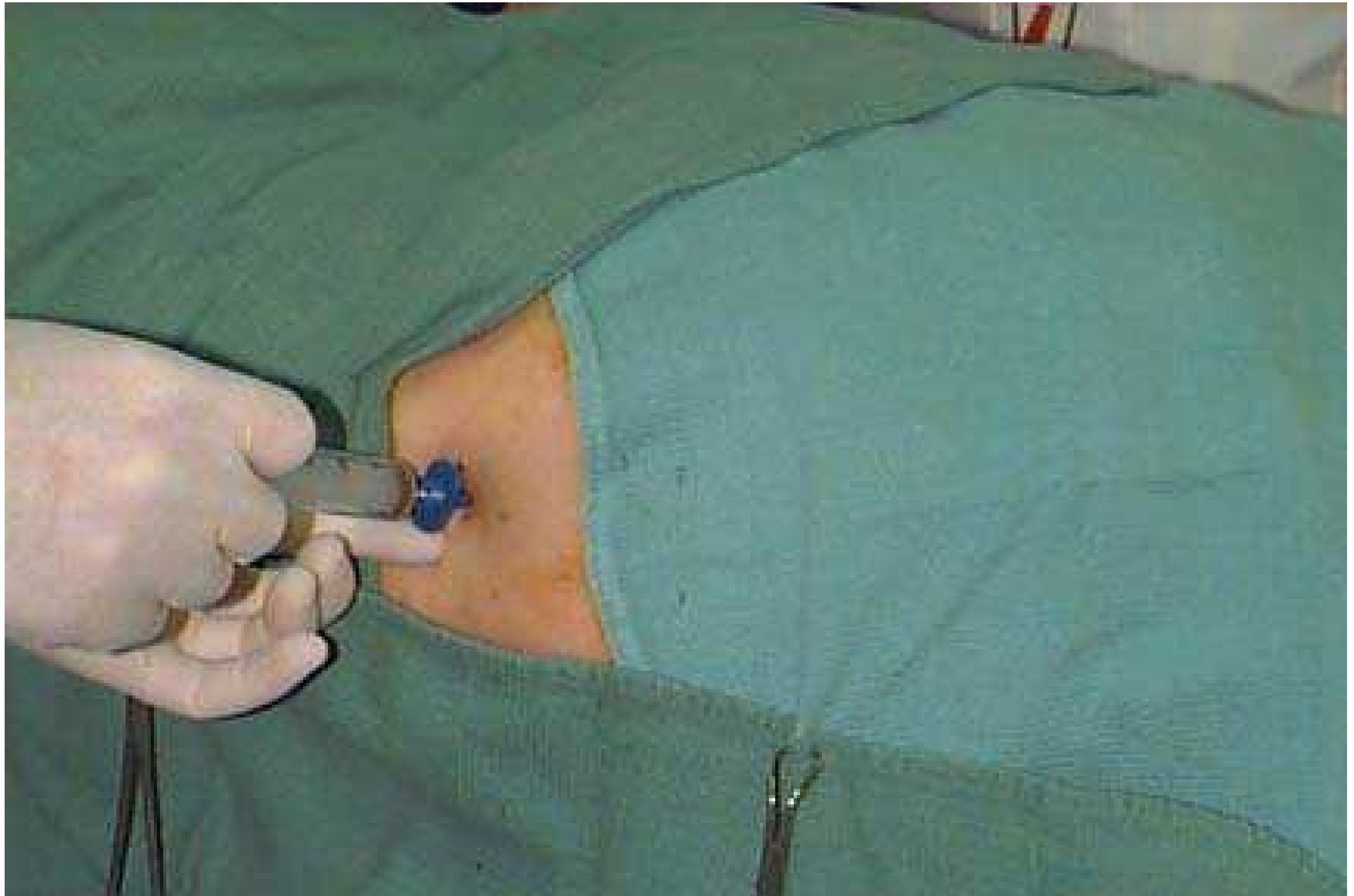
- 2010 Practice Parameters JCAAI, AAAAI, ACAAI

# The Con Position is that

- The prevalence of indolent systemic mastocytosis is very low in patients with anaphylactic shock or who have idiopathic anaphylaxis.
- Using a *screening criterion* of HYPOTENSION (anaphylactic shock) followed up with a *confirmatory test* by Bone Marrow Biopsy would result in a very high number of normal bone marrow biopsies.

# JCAAI, AAAAI, ACAAI Practice Parameters on Anaphylaxis

- "A bone marrow examination may be indicated in patients with a diagnosis of idiopathic anaphylaxis even in the absence of elevated tryptase levels if salmon colored, hyperpigmented macules and papules consistent with urticaria pigmentosa are found." JACI 2010 (Sept); e1-42.

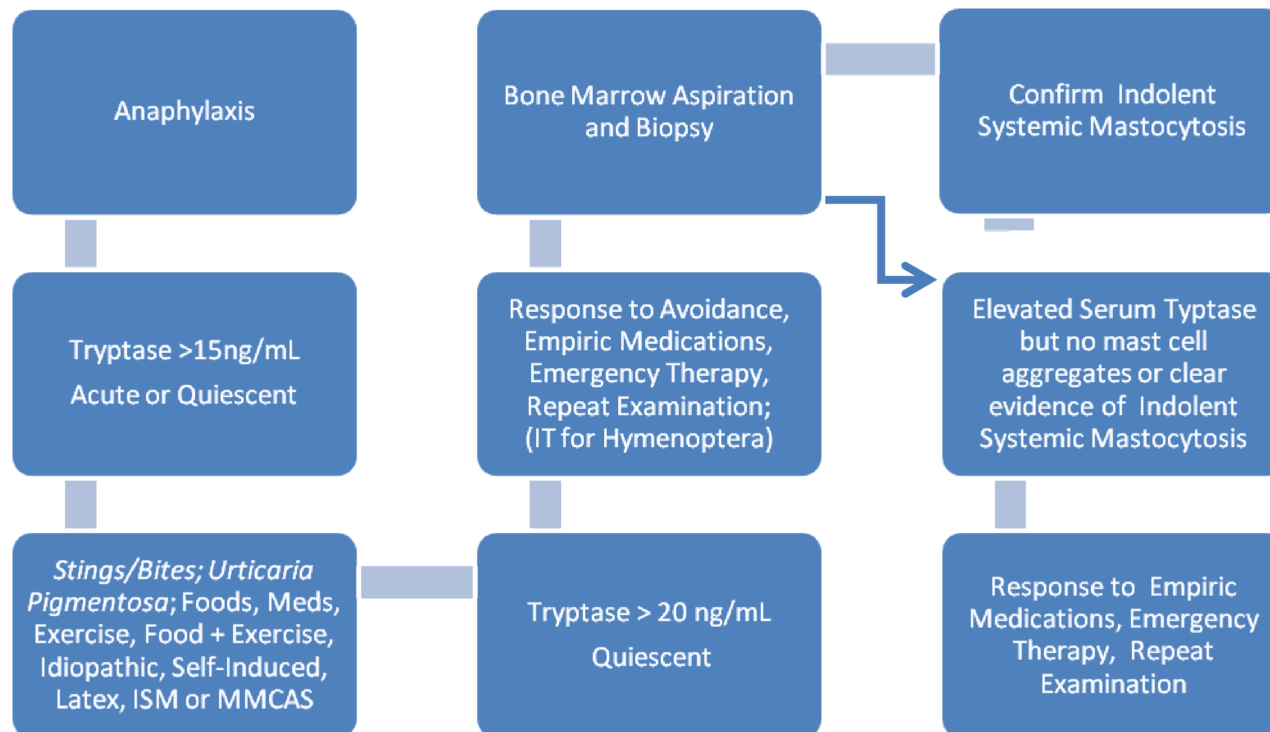


# Special Issues re the Procedure

- Failure to prevent, recognize, or initiate rapid response to excessive bleeding or, rarely, to an anaphylactic anesthetic event during the bone marrow sampling procedure
- Failure to identify complications in sampling an iliac crest that results in penetration of the underlying gastrointestinal tract as well as blood vessels—the latter which runs the risk of the development of massive retroperitoneal hemorrhage and gluteal compartment syndrome
- Thrombocytopenia/hemorrhage (not likely in patients with mastocytosis or anaphylaxis)
- Vasovagal reaction (patient or companion)

# Considerations in Planning

- Latex allergy
- Lidocaine “allergy” (10 ml of 1% injected)
- Povidone-Iodine allergy or rash
- Egg allergy if propofol considered
- Opioid “allergy” or intolerance (tramadol, fentanyl)
- Bleeding history or warfarin use
- Serious complications from bone marrow (0.05-0.07%)in non-mastocytosis patients
- Benefit to patient vs risks


Anaphylaxis
Bone Marrow Aspiration and Biopsy
Confirm Indolent Systemic Mastocytosis
Tryptase >15ng/mL
Acute or Quiescent
Response to Avoidance, Empiric Medications, Emergency Therapy, Repeat Examination; (IT for Hymenoptera)
Elevated Serum Typtase but no mast cell aggregates or clear evidence of Indolent Systemic Mastocytosis
Stings/Bites; Urticaria Pigmentosa; Foods, Meds, Exercise, Food + Exercise, Idiopathic, Self-Induced, Latex, ISM or MMCAS
Tryptase > 20 ng/mL
Quiescent
Response to Empiric Medications, Emergency Therapy, Repeat Examination

# Why Not?

- Unrecognized indolent systemic mastocytosis is unlikely in the absence of urticaria pigmentosa (not completely)
- Need to advise emergency therapy (epinephrine) and begin some empiric therapy anyway
- Determine if serum tryptase *remains* elevated; it may not and that favors another diagnosis than indolent systemic mastocytosis
- (In the History of Present Illness, record anaphylaxis following Hymenoptera stings)

# How Often is Indolent Systemic Mastocytosis Identified in Patients with Anaphylaxis?

- Idiopathic Anaphylaxis (Ditto A et al, Ann Allergy Asthma Immunol 1996;77:285-91): 0/335 and 0/335 cases of Urticaria Pigmentosa…1 pt had MGUS; 1 pt had total IgE that varied with episodes of IA. "Idiopathic Anaphylaxis implies a diagnosis of exclusion."
- Lieberman series (Memphis, TN) (Ann Allergy Asthma Immunol 2006;97:39-43): 3/601 (0.5%) patients identified. (*Patients with anaphylaxis from Hymenoptera stings and SCIT were excluded*).

# Diagnosing Indolent Systemic Mastocytosis in Series of Patients with Anaphylaxis (cont.)

- University center in Istanbul (Ann Allergy Asthma Immunol 2013;110:96-100): 2/516 (0.3%). No ICU care was required, but epi was administered. Idiopathic Anaphylaxis: 7 (1.4%)
- Bern (Clin Exp Allergy 2004;34:285-90) "Incidence of anaphylaxis with circulatory symptoms:……..comprising 940,000 inhabitants.." ("..about ½ of the Canton Bern is rural and "harbors twice as much beehives as any other canton…"

# Incidence of Anaphylaxis with Circulatory Symptoms

- Medical record review 1996-98 from 2 allergy clinics, 17 hospitals with EDs, 7 board certified in A/I.
- Inclusion criteria: severe anaphylaxis (hypotension, LOC, or shock) consistent with mast cell activation
- The diagnosis of anaphylaxis was made after A/I work up, skin prick tests, in vitro tests, some open challenges

# Severe and Life-Threatening Anaphylaxis

- Anaphylaxis in 215/7739 records
- Pattern of episodes of anaphylaxis:
  1 episode 214 (94.7%); 2 episodes: 9 (4.0%);
  > 2 episodes: 3 (1.3%).
- Causes: Hymenoptera (153) 58.8%;
  Drugs 41 (18.1%); Foods 23 (10.1%)
  Mastocytosis 1 (0.4%)
  Cold urticaria 1 (0.4%)
  Seminal fluid 1 (0.4%)

# In a Systemic Mastocytosis Center…
# Int Arch Allergy Immunol 2005;136:273-80)

- Retrospective review of 40 patients with ISM,
  severe life-threatening anaphylactoid symptoms occurred in 8 (20%) but only
  2 (5%) patients experienced such reactions BEFORE the diagnosis of ISM. (1 pt had no UP lesions; 1 pt had a few small MP lesions + on staining)

- All 8 patients had reactions to ant bites and yellow jacket stings.

# If I Fail to Obtain a Bone Marrow Examination In These Settings of Anaphylaxis

- Severe hypotension
- Hymenoptera sting reactions
- Recurrent episodes (of anaphylaxis without trigger)

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How serious are these conditions (ISM, MMCAS) if left undiagnosed (but presumably treated, at least in part, including self-injectable epinephrine for Hymenoptera stings)?

Osteoporosis, bone lesions, increased risk of serious hypotensive reactions, non-optimal pharmacotherapy

# The Con Position is that

- The prevalence of indolent systemic mastocytosis is very low in patients with anaphylactic shock.
- Using a *screening criterion* of HYPOTENSION followed up with a *confirmatory test* by Bone Marrow Biopsy would result in a very high number of normal bone marrow biopsies.

# Clonal Mast Cell Disorders in Patients with Systemic Reactions to Hymenoptera Stings and Increased Serum Tryptase Levels (JACI 2009;123:680-6)