

[Episode 152: Keywords Part 7: MH and Hepatic Disease for the Basic Exam](#)

On this episode: Dr. Jed Wolpaw and Dr. Gillian Isaac

In this 152nd episode I welcome Dr. Gillian Isaac back for another 2 ABA keywords. We discuss malignant hyperthermia and the portion of hepatic disease that is covered by the Basic Exam. We'll do the portion covered by the Advanced Exam on the next keywords episode.

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Malignant Hyperthermia Testing

- Which of the following statements best describes testing for susceptibility to malignant hyperthermia (MH)?
 - o **Live skeletal muscle cells are required for testing**
 - o The MH gene is located on the X chromosome
 - Would be much more prevalent
 - o Muscle biopsy is appropriate in children younger than 1 year
 - o A normal serum creatine phosphokinase concentration eliminates the need for muscle biopsy
 - o Succinylcholine is used to stimulate muscle obtained on biopsy for MH
 - Halothane-caffeine (gold standard)
- Gene panel testing
- Autosomal dominant

MH Pathophysiology

- MH is believed to involve a generalized disorder of membrane permeability to
 - o Sodium
 - o Potassium
 - o **Calcium**
 - o Mag
 - o Phosphate
- Motor afferent: Ach to motor end plate → initiate depolarization within sarcolemma T-tubules → open voltage-gated calcium channels → ↑ Ca in releases Ca in sarcoplasmic reticulum via **Ryanodine Receptor** (Calcium-mediated Calcium release)
 - o Site of MH
 - o Trigger binds receptor and goes right to Ca release → unmitigated contraction → dramatic increase in O₂ consumption, ATP depletion, production of heat. Membrane integrity failure.
- Muscle contraction stops when signaling ends

MH Triggers

- Two major triggers
 - o Halogenated anesthetic
 - o Succinylcholine
 - A 46-year-old man is scheduled for repair of an inguinal hernia. Six years ago, he had an episode of malignant hyperthermia during cholecystectomy. Which of the following is the most appropriate perioperative management?
 - o **Administration of a regional anesthetic**
 - TIVA is acceptable
 - o Administration of dantrolene orally for two days prior to surgery
 - Studies showed it doesn't help
 - o Avoidance of all inhalational anesthetics except isoflurane
 - No exception of halogenated
 - o Avoidance of ester local anesthetics
 - o Flushing the anesthesia machine with oxygen 10 L/min for a minimum of 12 hours
 - 10L/min for 20-104 mins
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- Change circuit, etc
 - Use charcoal filters
- Drugs suitable for patients with MH include all except
 - Etomidate
 - Nitrous oxide
 - Calcium chloride
 - Ketamine
 - **All of the above**

Syndromes associated with MH

- Which of following is not associated with MH?
 - Central Core Disease
 - Multimimicore
 - **Duchenne muscular dystrophy**
 - Unexplained cardiac arrest after succinylcholine in peds most likely DMD
 - King Denborough Disease
- ± hypo/hyperkalemic periodic paralysis

MH Presentation/Treatment

- Takes hours, may not see until postop
- Increased ETCO₂, temp, potassium
- Tachycardiac, HTN
- Respiratory acidosis, metabolic acidosis
- Myoglobinuria, fever
- Key differentiation of MH from NMS, serotonin syndrome:
 - sustained muscle contraction
- Treatment
 - 2.5mg/kg dantrolene + supportive
- Most sensitive early sign of MH during general anesthesia?
 - Tachycardia
 - Hypertension
 - Fever
 - **Increased PECO₂**
 - Hypermetabolic, thus will see this as well as metabolic acidosis early
- MH and NMS share each of the following characteristics except
 - Generalized muscle rigidity
 - Hyperthermia
 - Effectively treated with dantrolene
 - Tachycardia
 - **Flaccid paralysis after vecuronium**
 - Can differentiate by testing paralysis
- Not consistent with Dx of MH?
 - PaCO₂ 150mmHg
 - **MVO₂ 50 mmHg**
 - Expect to be much lower around 20-30 mmHg
 - pH 6.9
 - Arterial O₂ saturation 85% on 100% FiO₂
 - onset of symptoms hours after end of operation

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- Shortly after induction of GA for procedure, you suspect MH, which of following emergency treatment is most consistent with MHAUS?
 - o **Treat hyperkalemia with CaCl**
 - o Dantrolene IV dose not to exceed 1mg/kg
 - Correct dose is 2.5mg/kg
 - o Treat tachyarrhythmias with CCB
 - Doesn't work
 - o Pack patient with ice to achieve core temp < 36
 - No need to be hypothermic
 - Near end of 3-hr colectomy, surgeon complains patient not relaxed. 2 twitch monitors show zero twitches. Blood gas: pH 6.9/ CO2 86 / K 4.6 / acetate 4.6. Most appropriate action?
 - o Administer more vecuronium
 - o Administer bicarbonate
 - o Administer succinylcholine
 - o Increase minute ventilation
 - o **Administer dantrolene**
 - Patient appears relaxed but is rigid. Concerning for MH, so give dantrolene.
 - Not perfect picture but profound metabolic acidosis. If you suspect it, give it.

MH and Masseter Muscle Rigidity

- MMR and spasm after succinylcholine administration signals onset of MH in what % of patients?
 - o <50%
 - 25-30%
 - o 50%
 - o 65%
 - o 80%
 - o >80%

MH timing

- 5-year-old boy anesthetized for ambulatory procedure with GA and sevoflurane, N2O, oxygen via mask. On conclusion of procedure, taken to recovery. Before discharge, patient's urine is dark brown. Most appropriate action?
 - o Discharge w instructions to return if urine color does not normalize
 - o Discharge in 3 hours if no other sign/sx manifested
 - o Obtain serum creatinine and blood urea nitrogen levels and discharge if normal to rule out acute tubular necrosis
 - o **Rule out MH**

Summary

- Halothane-caffeine is gold standard for testing
 - Defect due to intracellular calcium stores preventing muscle relaxation
 - Defect in ryanodine receptor
 - Known triggers: halogenated anesthetic and succinylcholine
 - Association with Core syndrome, Multimimicore, King Denborough
 - Hypertension, tachycardia, acidosis, muscle rigidity, myoglobinuria, fever
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- Diagnosis unlikely if only one sign manifested
 - Lots of overlap with other hypermetabolic states
 - Treat w dantrolene 2.5mg/kg
 - MMR after succinylcholine associated with MH 25-30%
 - Can happen in recovery phase of care

Hepatic System: Dual blood supply

- Hepatic artery
 - o Aorta → celiac → hepatic
 - o 25% of blood flow
 - o 50% of O₂
- Portal vein
 - o From digestive tract
- Vessel rich group receives what percentage of cardiac output
 - o 45%
 - o 60%
 - o **75%**
 - Brain, heart, liver, spleen, endocrine
 - 10% of weight
 - o 90%
- Liver receives what % of cardiac output
 - o 15%
 - o **25%**
 - o 50%
 - o 75%

Hepatic blood flow and oxygen supply regulation

- Two demands
 - o Regulate oxygen for own maintenance
 - o Vital service to rest of body
 - Intrinsic regulation – hepatic arterial buffer response
 - o By adenosine
 - o Limited by things like portal venous pressure
 - Extrinsic regulation – by metabolic state
 - o ↓ pH, pO₂, ↑ pCO₂ of portal blood → ↑ hepatic artery flow to sustain metabolism
 - The following decreases hepatic artery blood flow except
 - o isoflurane
 - vasodilate
 - o spinal
 - vasodilate
 - o **hypercarbia**
 - o mechanical ventilation
 - o PEEP
 - Which of following most likely to increase hepatic blood flow during GA?
 - o PEEP
 - o Stop isoflurane and start enflurane
 - o **Increase PaCO₂**
 - o Moderate controlled hypotension
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- Subarachnoid administration of morphine
 - Hepatic acinus region is roughly divided into 3 zones that corresponds with distance from arterial blood supply. Which of following likely to be damaged as result of acetaminophen overdose?
 - **Zone 1**
 - Functional unit of liver. Closest is Zone 1. Best oxygenated, so first exposed from intestines. Zone 3 furthest so most susceptible to hypoxia
 - Zone 2
 - Zone 3
 - All

Liver function tests

- Healthy women undergoing arthroscopy with spinal anesthesia to T4. Which findings least likely
 - ↓ HR
 - At level of Cardioaccelerating fibers
 - ↓ hepatic blood flow
 - From vasodilation
 - ↓ MAP
 - ↓ TV
 - Diaphragm is fine
 - Hyperperistalsis
 - Unopposed parasympathetic
 - Hepatic damage
 - LFT
 - Bile flow
 - Alkaline phosphatase
 - Bilirubin
 - Hepatic synthetic function
 - Albumin
 - Prothrombin time
 - Metabolic flow and acid/base
 - 65-year-old man w hx of alcohol abuse. Which preop serum provides best assess of hepatic synthetic function?
 - **Albumin**
 - Alkaline phosphatase
 - Bilirubin
 - Globulin
 - Transaminase
 - 50-year-old man with jaundice scheduled to undergo inguinal hernia repair. Increase in which of following best indicates impaired hepatic function?
 - PT
 - Sensitive because short half-life of F7. Thus progressively rise is poor prognostic sign in likely acute hepatic failure
 - ALT
 - A:G ratio
 - Alkaline phosphatase
 - Bilirubin
 - In adult, liver is common organ for
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- Hb synthesis
 - Fetal mostly, but adults are mostly bone marrow. 20% liver
 - Hb degradation
 - RES
 - Factor 8 synthesis
 - 4 factors including proteins C/S, antithrombin-3, but not factors 3,4,8
 - Antithrombin3 synthesis

Drug metabolism is primarily hepatic event

- 70kg 20-year-old athlete receives nitrous, oxygen, fentanyl 1.25mg (25 mL) during 3-hour reconstructive surgery. Does not awaken or resume spontaneous breathing. Most likely explanation for prolonged effect of fentanyl?
 - Dose dependent elimination half-life
 - Correct term is “context-sensitive half-life”
 - Genetically slow biotransformation
 - Large volume of distribution
 - Presence of active metabolite in high concentration
 - Irreversibly eliminated by hepatic clearance
 - **Time required for hepatic elimination**
 - Plasma half-time of which of following is prolonged in patients with end stage cirrhotic liver disease?
 - Diazepam
 - Pancuronium
 - Fentanyl
 - **All**
 - Pseudocholinesterase:
 - Increased in patients with myasthenia gravis
 - Inhibited by glycopyrrolate
 - No, but neostigmine can
 - Inhibited by pilocarpine
 - **Synthesized by liver**
 - Severe liver disease → decrease in cholinesterase enzyme
 - Reverse atracurium blockade
 - Compared to patient without liver disease, patient with liver disease will have
 - **Greater accumulation of vecuronium w infusion**
 - More frequent occurrence of phase 2 block after succinylcholine
 - Prolonged elimination half-life of atracurium
 - Hoffman-elimination
 - Unchanged Vd of pancuronium
 - Patient with jaundice, minimally elevated AST, markedly elevated alkaline phosphatase, normal PT received muscle relaxant. Which of following is most likely?
 - Increased intubating dose of pancuronium
 - Increased intubating dose of atracurium
 - Prolonged duration of succinylcholine
 - **Prolonged duration of vecuronium**
 - Shortened duration of tubocurarine
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Summary

- Dual blood supply
 - Blow flow and oxygen supply regulated to meet demands
 - Intrinsic autoregulation – hepatic arterial buffer
 - Broad tests for liver function
 - Drug metabolism primarily hepatic
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References

Malignant Hyperthermia Website: www.mhaus.org

Great review website where Dr. Isaac gets her questions: <http://www.anesthesiahub.com>

Atlantic Article: <https://www.theatlantic.com/entertainment/archive/2012/03/what-do-fact-checkers-and-anesthesiologists-have-in-common/253838/#note>

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