There are a few key messages I want you to get out of this talk:

1. I can’t overemphasize the role of team performance in responding to a malignant hyperthermia crisis. Your knowledge and actions as individual members of a team make a difference. You’ll see this when I discuss a case of an actual MH crisis in one of my patients.

2. Malignant hyperthermia is one of the most feared crises in anesthesia. I want you to appreciate that although MH is rare it could happen to any one of our patients who have a general anesthetic. A plan of action is essential.

And finally, 3. I want you to understand the critical importance of getting the “antidote” dantrolene into the patient as quickly as possible - you are essentially racing to get the drug in before the patient arrests.

First I’ll talk about the who, what and hows of MH (as in: who’s at risk, what it is, how to recognize it and how to treat it.)

And by way of background for the case I’ll be presenting I’m going to talk a little bit about the goals of care for a head-injured patient. I hope that this will explain why MH is REALLY bad in a head-injured patient

And then I’ll present the case of a young man I took care of last summer.

MH is a hypermetabolic state (a biochemical chain reaction) triggered by certain anesthetic drugs in the muscle of susceptible individuals

As I mentioned earlier it is one of the most feared crises in anesthesia because even when treated appropriately it can be fatal.

It is rare. The incidence is estimated at between 1 in 50 to 65 thousand (some sources say as low as 1:100000). In some geographical hotspots, the incidence is as high as 1 in 5000 (Wisconsin, Nebraska, West Virginia and Michigan).

It is inherited in an autosomal dominant pattern so if you are a sibling or a child of someone with MH then there is a 50% chance you are also susceptible.

And here’s something I really want you to know: ANY of our patients could have an MH crisis - it doesn’t matter if they’ve had one or many previous uneventful GAs! It could happen at any time to any one. All of our patients are at risk.
I’d like to highlight some muscle physiology to set the stage for understanding the signs of an MH crisis (i.e., where they come from) and where the drug used to treat the underlying cause of MH acts (i.e., where you need to deliver it for it to work)

This is a drawing of a muscle going from it’s gross appearance down to it’s smallest functional units (the actin and myosin myofilaments).

Muscle contraction and relaxation requires the control of calcium within the muscle cell (i.e., making it available around the myofilaments to cause contraction and taking it away from around the myofilaments to cause relaxation).

Signals from the brain reach the muscle fibers via motor neurons.

The sarcoplasmic reticulum is basically a big bag of calcium and it is what controls where the calcium is in the cell - available or contained. THIS is where the pathology is in MH.

So in normal muscle contraction and relaxation...
An electrical signal travels along the motor neuron...and causes the release of calcium from the sarcoplasmic reticulum. When calcium bathes the myofilaments...they pull against each other and the muscle contracts. As long as calcium is present around the actin and myosin filaments, the muscle remains contracted.

For the muscle to relax...
...the nerve impulse stops. Calcium channels close in the sarcoplasmic reticulum and calcium is pumped back into the sarcoplasmic reticulum and the myosin and actin filaments return to their relaxed state and the muscle relaxes.

However, in the case of MH Induced Rigidity.....a triggering agent (one of the volatile anesthetic agents including isoflurane, sevoflurane, desflurane or the muscle relaxant succinylcholine) acts at a dysfunctional calcium channel receptor on the sarcoplasmic reticulum and causes it (the calcium channel) to remain open (i.e., it makes it ‘stick’ open)...

...this causes the sustained release of calcium. And remember as long as calcium is around the myofilaments of the muscle.......it will stay contracted. Or rigid.

Rigidity is one of the first signs of an MH crisis.
These muscles are working hard. And this hypermetabolic state causes the generation and release of... CO2. High CO2 (hypercarbia) is another early sign of an MH crisis. These muscles also generate... Heat.

The body responds to the workload of the muscles by delivering more oxygen to them. This increased cardiac output is manifested in......increasing heart rate.

The working muscle consumes......energy. And at some point the muscle cells’ energy will......be inadequate for aerobic metabolism and the cells will produce......lactate...When the cells’ energy stores are completely depleted...muscle cells die and their cell membranes rupture......spilling massive amounts of potassium into the bloodstream. Cell death also results in the release of muscle pigment (myoglobin) into the blood which is toxic to the kidneys.

So you’ve got rigidity, tachycardia......hyperthermia......acidosis (both respiratory from the high CO2 and metabolic from lactate) and.......hyperkalemia.

These are the signs...
...of an MH crisis

Treated or Untreated, the results of the hypermetabolic state can lead to kidney failure, liver failure, bleeding, cardiac arrest, death

The most immediate threat to life is hyperkalemic cardiac arrest.

So again, to review in an MH crisis...

A triggering agent causes the sustained release of calcium from the sarcoplasmic reticulum leading to: muscular rigidity, rising CO2, tachycardia, rising temperature, acidosis, cell death and resulting hyperkalemia and myoglobinemia and myoglobinuria (dark coloured urine).

So what should you do when you recognize an MH crisis?

Get help. You’re gonna need lots of it to put out this fire. This will become clearer as we talk about what you need to do to treat the underlying cause of MH.
So the first thing you do is get help. Next?

Get the MH cart. It has the materials you need to treat a crisis.

Next?

Remove the trigger. In an established anesthetic that means turning off the vaporizer and turning on high flow oxygen (i.e., 15 liters per minute) and not using succinylcholine.

Don’t waste time changing the circuit. You are racing against a potential hyperkalemic cardiac arrest.

So remove the trigger.

That in itself will not stop the MH reaction. To stop the reaction we need to get the calcium back into the sarcoplasmic reticulum. And we do that by...

...giving the specific antidote: Dantrolene.

It works by closing the ‘stuck open’ calcium channels in the sarcoplasmic reticulum...allowing the calcium to be pumped back into storage

...allowing the calcium to be pumped back into storage and thus stopping the uncontrolled muscle contraction.

So that treats the underlying cause of the crisis but we still have to deal with the consequences of the previous hypermetabolic state. That is...

...we need to treat the hyperkalemia and acidosis, cool the patient (because the body’s enzyme systems are designed to operate within a very narrow range of temperature), and protect the kidneys from damage by muscle pigments from dead muscle cells.

So again, to review...

...the signs of an MH crisis are... rigidity, tachycardia, hyperthermia, hypercarbia, lactic acidosis, hyperkalemia

And the critical steps to treat a crisis are...
And the materials we need to do this are in the MH cart...

Do you know where your’s is?

So you’ve summoned help and you’ve got the cart in the room...

...by this time you’ve removed the trigger.

It is crucial to get enough dantrolene to the patient’s muscles to stop the reaction BEFORE cardiac arrest happens (you’ve got to get the drug to its target (the muscle) and ideally that’s before you start compressions!)

Each vial of dantrolene (20mg) must be mixed with at least 60cc of sterile water.

The initial recommended dose is 2.5mg/kg. Lets just say we have the “typical” 70kg patient.

That’s almost **nine vials** of dantrolene and **over half a liter** of solution!

And it may take up to 4 times that much! As many as THIRTY-SIX vials!
I’d like to point out that each vial of dantrolene contains 3g of mannitol (for isotonicity) and that’s good because it’s an osmotic diuretic and helps protect the kidneys.

Our MH cart has equipment to help reconstitute the dantrolene quickly...

...on the top of our cart there is a supply of a special syringe system called the Cornwall Syringe System...

...Here’s a picture of one.

MH Cart.

It allows you to spike a bag of sterile water, draw up a set volume (usually 10cc) by drawing up on the blue lever, deliver that volume to the vial of dantrolene and repeat this 5 or more times to get 60cc into the vial. (without having to connect and disconnect the syringe from the bag and vial individually)

The top of our cart also has...

... a handy MH checklist (at this point I should mention that there is an MH hotline staffed by anesthesiologists of the Malignant Hyperthermia Association of the United States that can be called for advice regarding emergency management)
The MH cart also contains supplies to treat the biochemical fallout...

...specifically to treat hyperkalemia (insulin syringes and dextrose), acidosis (bicarb) and and to induce diuresis to protect the kidneys(furosemide)

Assessing the effect of these interventions is critical and so the cart contains...

Supplies to place invasive monitors (arterial line kits, central line kits) and send serial blood samples to monitor serum potassium and blood gases (grouped in handy bunches of vials corresponding to a bloodwork mnemonic)

Cooling the patient is the next priority...
...and the cart has supplies for gastric and bladder lavage with cooled fluid.

The most effective way to cool a patient is with bags of ice applied to the skin. Using a forced air blanket on “ambient” is also useful.

So that’s the MH cart

Now I’d like to talk about the case of a young man I took care of last summer....

The patient was a young man with a history of asthma who was an unbelted passenger in a high speed car versus tree crash. He had a severe head injury with a depressed right parietal skull fracture and no other injuries.

Before I talk about the details of his care...

I’d like to make a few points about head injury and the priorities for taking care of head-injured patients. My hope is that you’ll appreciate why MH in this particular patient was troublesome.

Here’s something you already know...

The skull holds brain, blood and CSF.

And at least in the adult...

...the skull volume is fixed...

...and here’s the inconvenient thing (for head-injured patients)......injured brain swells

This is a problem because if you try to increase the volume of stuff in the skull, the pressure inside the skull goes up. As that pressure goes beyond a certain level blood flow (and hence oxygen delivery) goes down and this causes injury and death of brain cells.

Fortunately the body can compensate for a little bit of brain swelling by......moving CSF from in and around the brain out of the skull and down around the spinal cord...
...unfortunately this displacement of CSF has limited ability to compensate volume-wise for the swelling of injured brain......

....fortunately we (as doctors and nurses and RTs) can influence the volume of blood in the skull by controlling CO2 (ventilation). Cerebral blood flow (hence volume) varies linearly with arterial CO2 over a certain range. And so by......hyperventilating and getting the arterial CO2 down to around 25mmHg we can reduce the blood volume in the skull and make room for swollen injured brain...

My main point here is that in a head-injured patient... It is critical to keep CO2 low and maintain MAP

When I assessed this patient in the ICU before surgery he was intubated and ventilated. He was sedated and moving 3 of 4 limbs. **His heart rate was 81 and his initial potassium was low at 3.4**

Just prior to transfer from the ICU to the operating room......I gave him rocuronium (a muscle relaxant) and midazolam (neither of which are triggers for MH)......the first half hour in the operating room (1015 to 1045) was spent placing an art line and central line and positioning the patient. The first indication that things weren’t right was......difficulty ventilating (high airway pressures, rising CO2)

He had asthma so bronchospasm was possible so I gave him some ventolin...

My main focus for him was ventilation and I had great difficulty hyperventilating him due to high airway pressures. As I was struggling to do this... The second sign (high temperature) presented. This was a trauma patient (if anything he should have been HYPOthermic with a temperature of 33 and change degrees) This didn’t make sense and I asked myself ‘is this MH’? With the onset of tachycardia (over several hours from 80 to 140/min) I wondered if this might be a drug ingestion.

I should mention that fairly early on we actually had to reposition the patient’s head so that I could ventilate (I couldn’t even pass a suction catheter through the endotracheal tube because was rigid and had curled his body up and flexed his neck enough to kink the tube) - this was only clear in retrospect because the patient was fully covered by drapes and an overbed table

...the sign that pointed most to a diagnosis of MH was......the massive increase in serum potassium and a developing acidosis

The patient was on his way to a hyperkalemic arrest.

What did we do?

We did everything right.
I stopped the volatile and turned up the flows. I swear from the time I said “This is MH get help and get the MH cart” it was but seconds before the MH cart and then 2 of my colleagues arrived. Shortly after, the first syringe of dantrolene was in my hand and in the patient. And the syringes kept coming - 12 for the first dose and then another 12 before we transferred the patient to the ICU. We gave bicarb. We cooled the patient.... We followed the chemistry and gases.

Let’s look at the record...

Triggering agent OFF, high flow oxygen... Dantrolene 240 + 240 mg, bicarb, calcium. (Anyone wonder why we gave calcium? - MH is a disorder of INTRacellular calcium regulation; IV calcium is part of the ACLS protocol for HYPERkalemia) We switched the forced air to ‘ambient’ and put ice on the patient. The heart rate started coming down with the first dose of dantrolene. You can see it started to come back up between the first and second doses.

The potassium came down and the acidosis resolved prior to transfer to the ICU.
He was hemodynamically stable and his temperature was 38.8 on arrival in the ICU (the peak in the OR was 39.3)

I’d like to take a moment to recognize the members of the team (nurses and HCAs) who helped me respond to this crisis. And I’d like to say that as an anesthesiologist one of the qualities I most appreciate in the nurses I work with is what I’ll call ‘situational awareness’ - the ability to observe and intuit (without being specifically told) that I am worried about a patient or developing situation. The nurses with me that day all have that ability and use it. I appreciate it because it eliminates the step of me getting their attention and assistance when something really bad (for the patient) is happening or is about to happen. In an MH crisis response time matters.

As I mentioned earlier I can’t overemphasize the role of team performance in responding to a malignant hyperthermia crisis. Your knowledge and actions as individual members of a team make a difference.
And we did.....I’m happy to report that I met this patient and his dad in the hospital coffee shop 2 months after his injury. I sat down and had a conversation with him. He bragged that he’d just walked 300m! An amazing result.