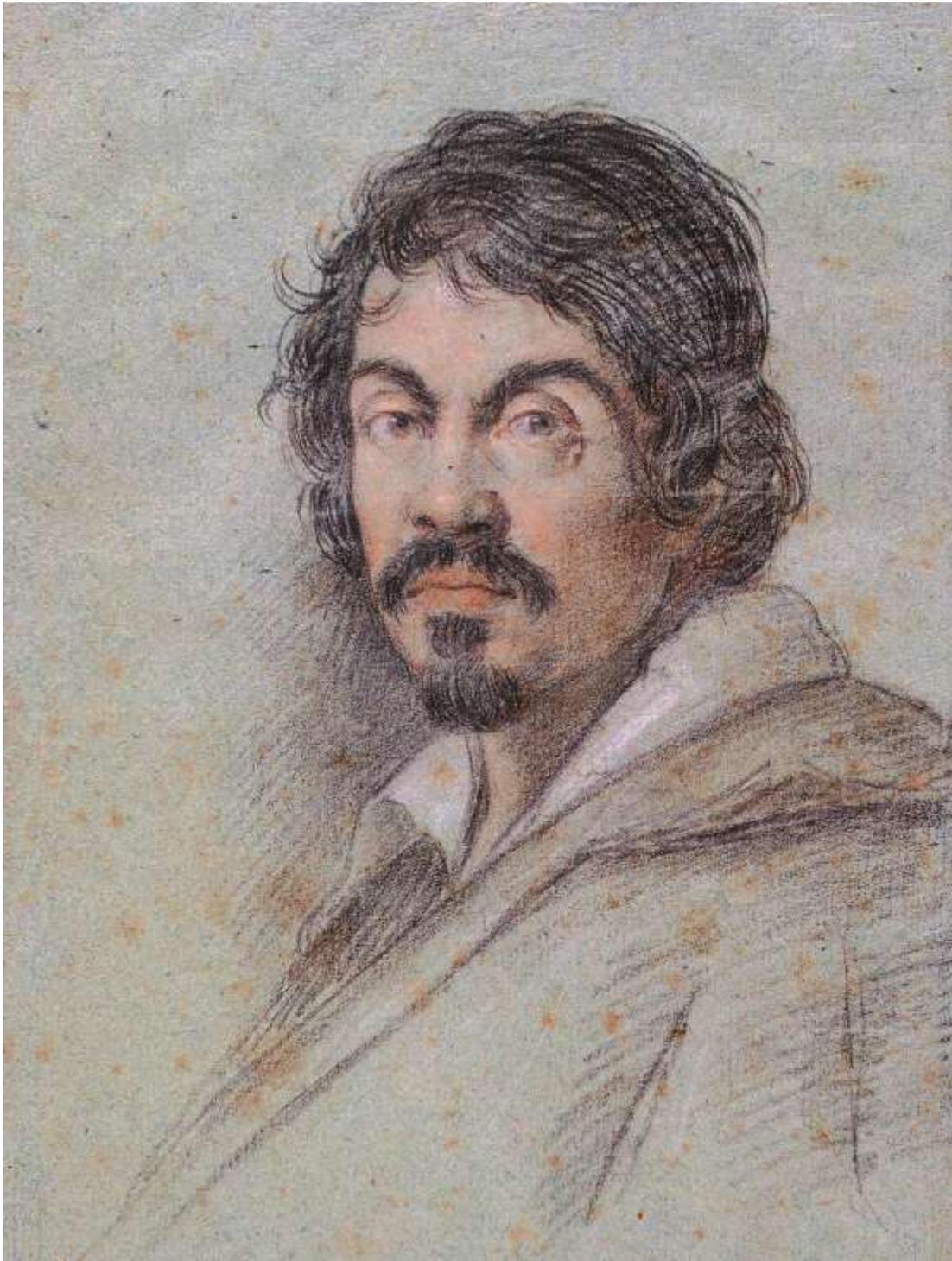


DANTROLENE



“Without hope, without fear”; “Portrait of Caravaggio”, charcoal on paper, 1621, Ottavio Leoni. (Biblioteca Marucelliana, Florence).

Rome. 1600.

The center of the greatest propaganda campaign Christendom has ever seen.

The Catholic Church is under siege from the Protestants of Northern Europe, who have a new message for those in need of salvation. "Just depend on the Word", said the Protestants, "the gospel truth in black and white. A printed bible is a Christian's guide. Paintings in churches are a distraction, filthy idols. Wipe them out".

Catholics shot back - "What about the millions who can't read? Don't they deserve to be saved? Shouldn't the poor have a vision of the sacrifice of the savior? The life of the virgin?"

In the Catholic churches' war for souls paintings were not art objects.

They were the heavy artillery.

So churches are repaired, others newly built, all lavishly decorated with paintings, the paintings responsible for defending the Catholic faith.

But away from the Vatican, outside the gorgeously decorated high-walled palaces of the aristocratic cardinals, there was a very different Rome.

The Rome of the sweaty, yelling crowd.

A hundred thousand of them, jostling in the markets, in the piazzas, the Rome of sour wine, old garlic, street urchins, shifty part-time soldiers who cut your purse, or your throat, just as soon as look at you.

The Rome of beggars, buskers, tumblers, quacks and whores, thousands of them working away in the ortaggio, the evil Eden, down by the River Tiber.

This was Caravaggio's Rome. Cheap rooms and drunken nights with other perpetually broke painters. Living on their wits and shady credit, art for butter, always on the fly.

*Their motto as they prowled the streets - **nec spe nec metu** - without hope, without fear.*

Simon Schama, "The Power of Art", BBC 2006.

Lost on 21st century sensibilities, the Baroque style of the of the early Seventeenth century, was not simply about bible stories. It was propaganda to win hearts and minds in a titanic struggle. In the words of the magisterial Simon Schama, it began as the "heavy artillery" in the prelude to one of the most destructive conflicts in human history, before the time of the French Revolution and the Napoleonic Wars - The Thirty Years War - the greatest war in history fought by both belligerents in the name of religion.

The Protestant Reformation would be led by a fierce iconoclasm and a revised and vernacular bible. This was fine for the elite, but the majority were still illiterate. The

Catholic response would be a far more sophisticated affair. In an age when the vast majority of the population were illiterate, religious images would be used as their means of propaganda. But the lessons to be conveyed to the masses could no longer be with images of idealized saints with misty eyes looking to the clouds and hands held in pious prayer in the Mannerist fashion - a new kind of Art would be required that conveyed a direct, earthy, and believable message, one that any mortal sinner could instantly identify with. The only trouble was, no one knew what this new Art should look like, let alone which Artist could even produce it.

*Then Michelangelo Merisi da Caravaggio was discovered. His Art was divinely inspired, his techniques, unsurpassed. He was one of the most naturally gifted Artists since his namesake of over a century past. There was only one problem, however. Caravaggio was fierce, ungoverned, volcanic and unpredictable. He lived among the desperate classes, who lived by the motto they scrawled on the buildings of the streets - **nec spe nec metu** - without hope, without fear. The cardinals agonized - "How can we possibly commission **this** man?" and in reply they told themselves "...yes, but just look at his work - no mortal is capable of doing what he does, surely god himself guides his brush - how can we not commission him!?"*

The only time we hear any words from Caravaggio himself is in the criminal court records of his not infrequent appearances. These records do give us some direct connection with the brilliant but flawed man. A 21st century psychiatrist looking at them could have some cause to ponder one of their favorite modern diagnoses - "antisocial personality disorder". In 1603 Caravaggio had penned a number of obscene poems about a mediocre artistic rival who had gained a commission over him, a certain Giovanni Baglione. Baglione got wind that the poems were "doing the rounds", he was outraged and the inevitable suite for libel quickly followed. No one had actually seen him write the verses, they were unsigned, but apparently it was "common knowledge".

The court prosecutor asked him who had written the obscene poems.

"Poems? What poems?", he replied.

And so one was read out to the court:

*....Giovanni Baglione, you're just a know nothing
Your pictures are just daubs
I warrant you won't earn
A brass farthing from them
Not enough for cloth to make breeches
So you'll have to go round
With your arse in the air....
In fact maybe you could wipe your arse with them
Or stuff them up Tommaso's (Baglione's friend) wife's hole.....and so on and so forth
in this (edited) vein...*

"Oh, those poems!", replied Caravaggio, (apparently laughing uncontrollably).

“I have no idea. They have nothing to do with me. But whoever wrote them is obviously a fine art critic!”

Nothing could be proven, and so Caravaggio walked free, escaping time in the galleys.

But the next year he was back in court again, following a serious assault on a tavern waiter named Pietro da Fusaccia, who had put a plate of eight artichokes in front of him, four cooked in butter, and four cooked in oil. Caravaggio asked which was which, and the waiter dismissively told him to smell them and work it out for himself. Caravaggio erupted. He screamed at the waiter, “Listen, becco fottuto, fucked over cuckold, do you think you are talking to some barone, bum?”. Evidently this was a rhetorical question. Caravaggio then repeatedly rammed the waiter’s face into the plate of artichokes and proceeded to draw his sword, but was restrained by his friends. Later on he was stopped by the sbirri (city watch) and challenged for carrying a sword without a license. He managed to satisfy them that as someone protected by the great Cardinal del Monte, he was an important person and so entitled to carry it. The officer let him go, and that would have been the end of it, until the officer wished him good night to which Caravaggio replied, “Ho in culo”, (up my arsehole). It was off the to the Tor (court) again for Caravaggio.

This was Caravaggio. The magisterial Simon Schama has perhaps best summed up his enigmatic genius; “There are only two things you need to know about Michelangelo Merisi da Caravaggio: that he made the most powerfully Christian art that has ever been painted; and that he killed someone”.

Though powerful patrons and protectors such as Cardinal del Monte struggled mightily and relentlessly to control the “collateral damage” they knew that in the great struggle for souls there was only one man who was able to connect with the ordinary people - Michelangelo Merisi da Caravaggio. And as it is that when we battle the condition Malignant Hyperthermia there is one and only one agent that can get the job done - Dantrolene. (.....and happily its possible collateral damage is minimal).

DANTROLENE

Introduction

Dantrolene is a **direct acting** skeletal muscle relaxant.

It is the specific drug of choice for the treatment of the life - threatening condition, malignant hyperpyrexia.

Administration of this agent is time critical.

See also document on Malignant Hyperthermia

Preparation

Tablets: 25 mg and 50 mg capsules.

Ampoules: Dantrolene sodium comes in **20 mg ampoules** as a powder for mixing with diluent, (60 ml of Water for Injection).

The **IV** form is used for malignant hyperthermia.

Pharmacokinetics

Absorption:

- Dantrolene is given IV for cases of malignant hyperthermia.
- It is given orally for cases of chronic spasticity

Distribution:

- There is some reversible binding to plasma proteins
- Dantrolene can cross the placenta

Metabolism and excretion:

- Dantrolene is metabolized in the liver.
- The mean biological half-life of dantrolene sodium after intravenous administration is about five hours.

Mechanism of Action

Dantrolene sodium is a direct acting muscle relaxant that acts specifically on skeletal muscle.

It does *not* affect neuromuscular transmission nor does it have measurable effects on the electrically excitable surface membrane

Dantrolene decreases the loss of calcium from the sarcoplasmic reticulum into the myoplasm and so uncouples the excitation and contraction of skeletal muscle.

Dantrolene given intravenously has no appreciable effect on the cardiovascular system or on respiratory function.

Indications

Indications include:

Definite:

1. **Malignant hyperthermia**

Less certain efficacy:

2. Neuroleptic malignant syndrome,⁴ (seek specialist Toxicologist Advice).

Outside of the setting of the ED/ ICU/ Anesthetics:

3. Chronic spasticity associated with spinal cord injury, head injury, MS, cerebral palsy or stroke (this is by oral therapy)

Contra-indications / Precautions

There are no true contraindications to dantrolene – which is life saving in cases of malignant hyperthermia

Pregnancy

Dantrolene is classified as a B2 drug with respect to pregnancy.

B2 Drugs are those which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.

It should be noted however that malignant hyperpyrexia is a lethal condition untreated and so Dantrolene must never be withheld, when required.

Breastfeeding

No data is available; avoid breastfeeding.

Adverse Reactions

These include:

1. Thrombophlebitis
 - Dantrolene solutions have a high pH.
2. Extravasation can result in tissue necrosis
3. Idiosyncratic or hypersensitivity liver impairment may be seen, (more with chronic oral use)

Dosing

IV dosing for malignant hyperthermia:

Administration of this agent is time critical.

- Give **2.5 mg / kg**, by **rapid IV** initial bolus into a large peripheral vein through a large bore catheter, (the agent is alkaline and very irritating).

Dantrolene comes in **20 mg ampoules**

*An average **9-10 ampoules** will therefore be required as an initial dose for an average 70 kg patient.*

- Doses can be repeated 10 minutely as necessary.
- There is **no** strict upper limit to the dosing of dantrolene; however in most cases symptoms are usually controlled with doses in the range of 5 -10 mg / kg.
- 1-2 mg/kg may need to be repeated IV 4 hourly for the next 24-72 hours.

Therapeutic end points

Dantrolene therapy continues until signs of hypermetabolism (acidosis, pyrexia, muscle rigidity) are resolved.

References

1. MH Resource Kit; RMH Department of Anesthetics:
 - www.anaesthesia.mh.org.au/mh-resource-kit/w1/i1002692/
2. Dantrolene in Australian Medicines Handbook, October 2013
3. Dantrolene in MIMs October 2013.

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