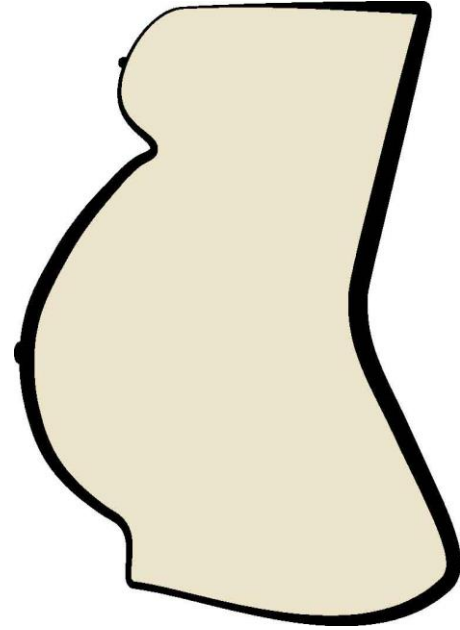




The pregnant woman with a neuromuscular disease

Gunilla Islander
MD, Associated prof
Intensive and Perioperative Care
Skåne University Hospital
Lund



My comment

Pictures on patients are not included in this pptx file

About rare diseases in general

Each rare disease is rare by definition.

The total number of patients with a rare disease is quite high, because there are many different rare diseases.



Neuromuscular and Anaesthesia and Pregnancy

Neuromuscular diseases can give problems
during anaesthesia and pregnancy

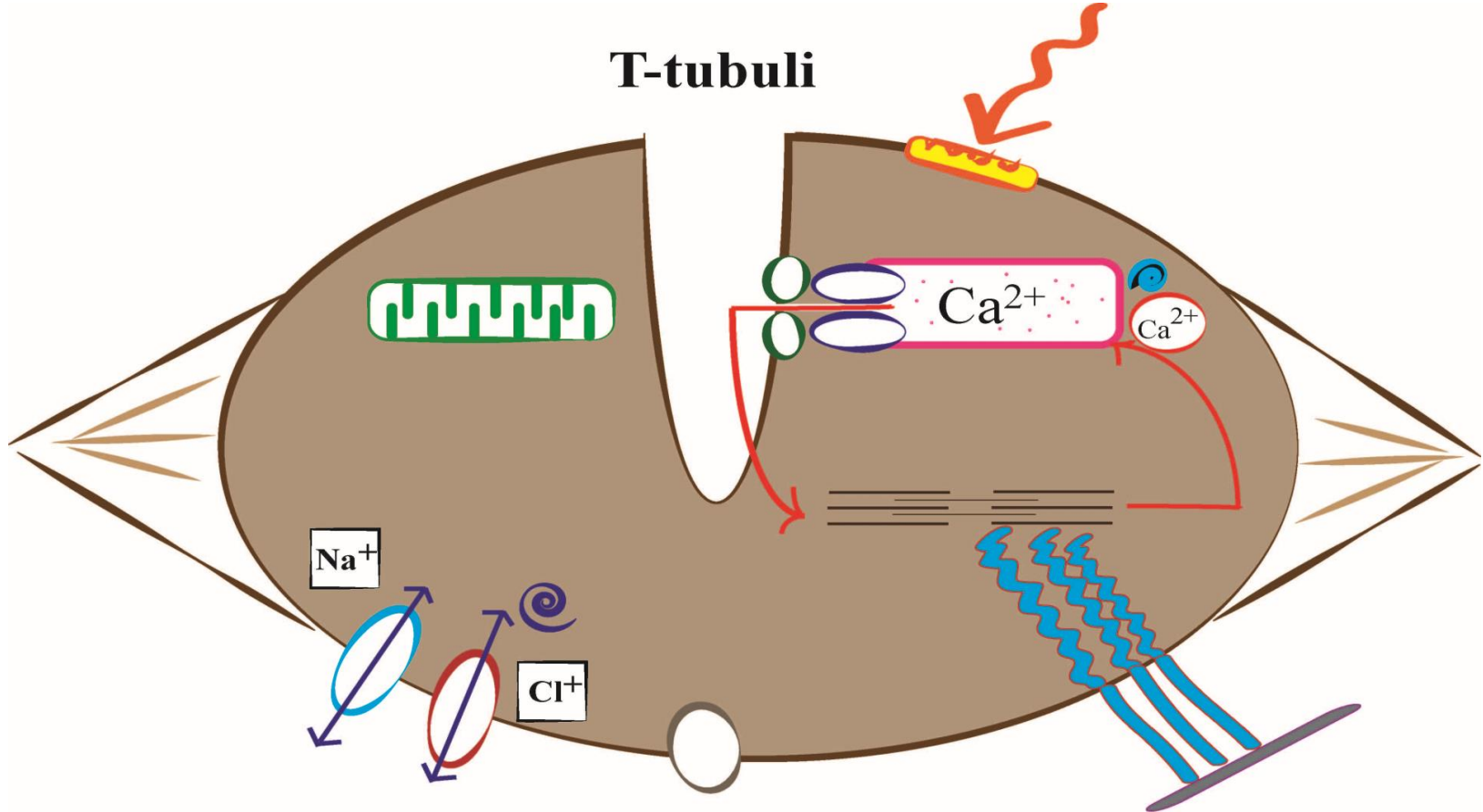
No robust statistics to lean on

(exception myotonic dystrophy and partly SMA)

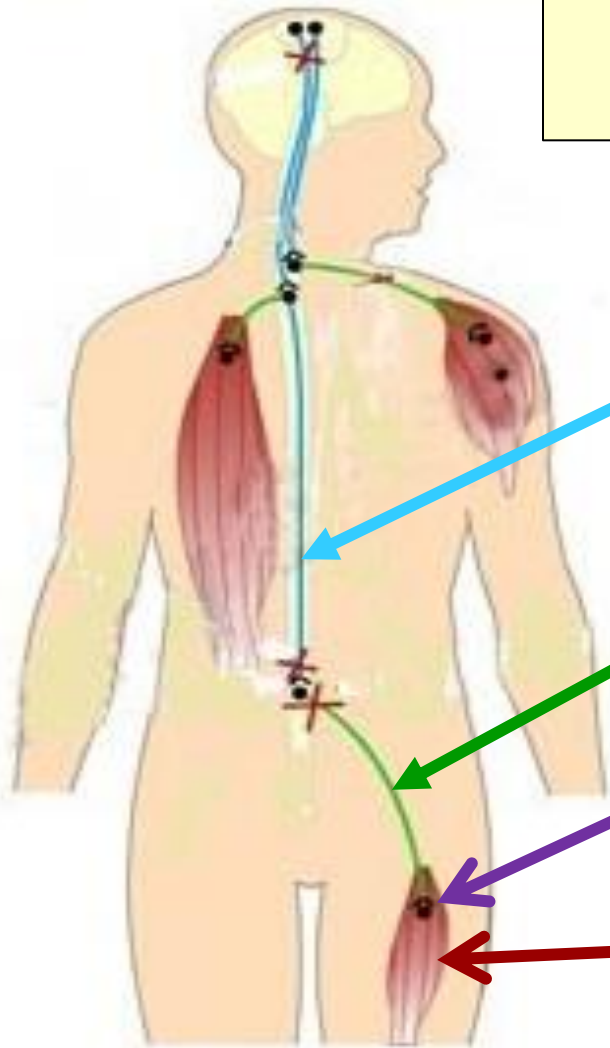
Advices are mainly based on;

- Oldfashioned case reports
- Case series
- Patophysiological knowledge
- Genetic knowledge
- **Common sense**

Muscle cell physiology for "dummies"



Neuromuscular apparatus



Neuron 1
Increased tonus etc

Neuron 2
Flaccid paraly (contractures)

Synapse

Metabolic very active and
"strong" organ. Different
types of symptoms

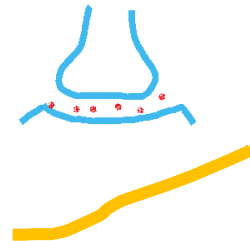
Muscle diseases

”geographical map”?

- **Myotonias**
- **Dystrophies**
- **Others**
 - Mitochondrial
 - Congenital myopathies
 -



-
- **Myasthenia gravis**
 - **Charcot Marie Tooth**
 - **Spinal muscle atrophy**



Some muscle disease can manifest themselves for the first time during anaesthesia/ pregnancy /labor.

Often as a disaster.

Hypermetabolic fever

MH

Generalised muscle rigidity or masseter spasm

Myotonias

MH

Mg²⁺ susceptibility

Myasthenia gravis,

Other neuromuscular diseases

Examples

Rhabdomyolysis

McArdles disease,
MH

Hyperkalaemic cardiac arrest during anesthesia

Duchenne/Beckers disease

A PART OF TAKE HOME MESSAGE

Genetics

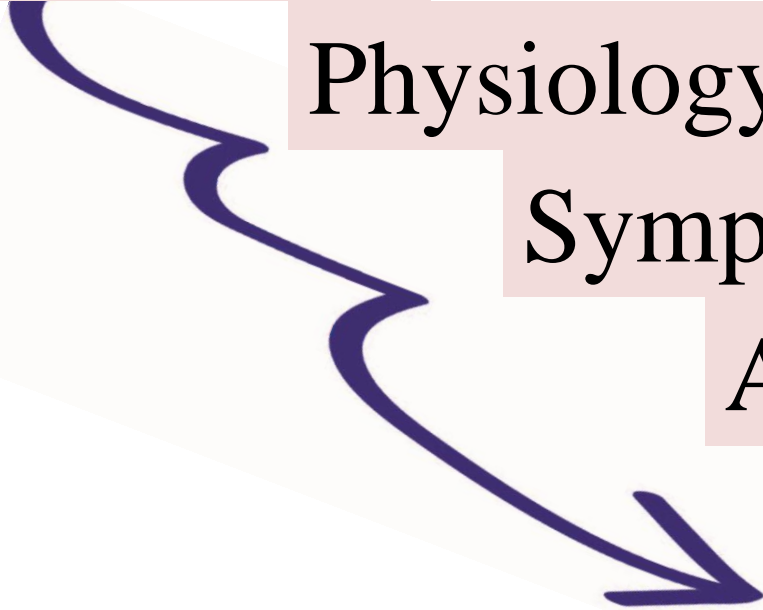
Sometimes it is like this

Physiology/Patophysiology

Symptoms/ Clinical pictures

Anaesthesia

Anaesthesia problems



Myotonic dystrophy

Myotonia, what is that??

**Myotonia is delayed
relaxation after muscle
contraction**

=

Attacks of stiff muscles



Myotonic dystrophy or Steinerts disease

- **Myotonic dystrophy I**
- Myotonic dystrophy II ("light" variant)

The name denotes that symptoms are both **dystrophic** and **myotonic**

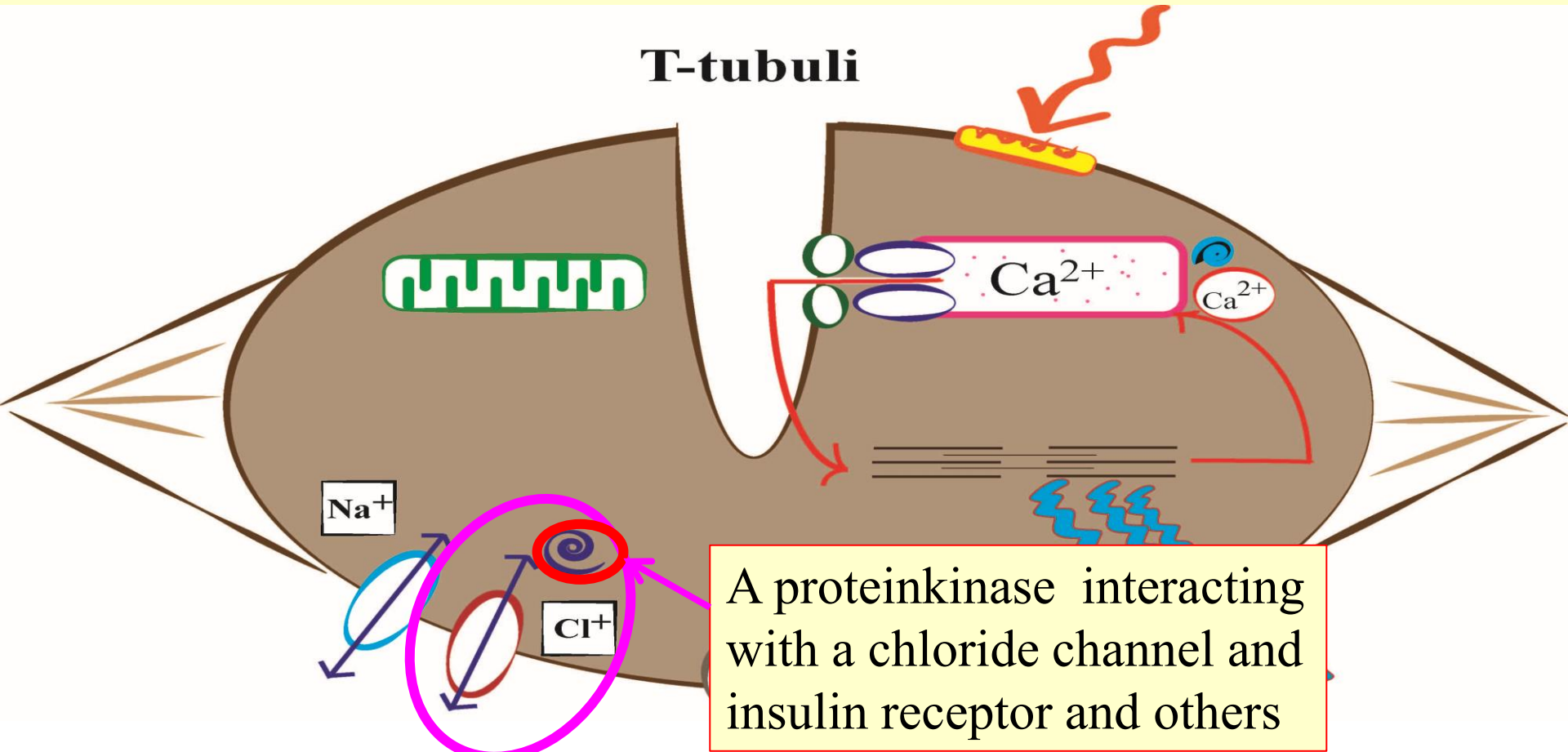
Myotonic dystrophy and GENETICS

AUTOSOMAL DOMINANT with anticipation and imprinting

ANTICIPATION Disease starts earlier for every generation

IMPRINTING Worse if inherited from the mother.

WHAT IS WRONG (physiology)? Myotonic dystrophy



T-tubuli

Na^+

Cl^-

Ca^{2+}

Ca^{2+}

A proteinkinase interacting with a chloride channel and insulin receptor and others

Myotonic Dystrophy symptoms

- **Muscles skeletal and smooth**

Weakness > myotonia

- **Heart arrhythmias, cardiomyopathy**

- **Gastrointestinal dysmotility. Uterus**

- **CNS**

- **Endocrine e.g. diabetes**

- **And many other symptoms**

IMPORTANT TO KNOW

- More than half of the patients are not aware of their disease (*anosognosia*). "Withdrawing" personality.
- If the patient is not aware of the disease, it is difficult for the anaesthesiologist to know about it.
- Anaesthesia complication can reveal the diagnose for the first time

Pregnancy & Labour

Pregnancy & Labor

Polyhydramnios	17%	***
Placenta anomalies	11%	***
UTI	9%	*
Preterm	31%	***
CS	37%	***
Instrumental	15%	*
Non-vertex	35%	***

Child affected

Obstetric risks are mainly, but not only, seen when fetus is affected

Case Myotonic dystrophy

- *Partus I* Normal vaginal delivery
- *Partus II* Emergency cesarean - placenta previa
- *Partus III* Emergency cesarean. Anaesthesia induction caused AF and circulatory failure.
 - Baby boy - floppy infant died after 5 days
- *Partus IV* Polyhydramnios, diabetes, small for age
 - Baby girl - Floppy infant, respiratory insufficiency, on ventilator.
 - Died after 7 months.

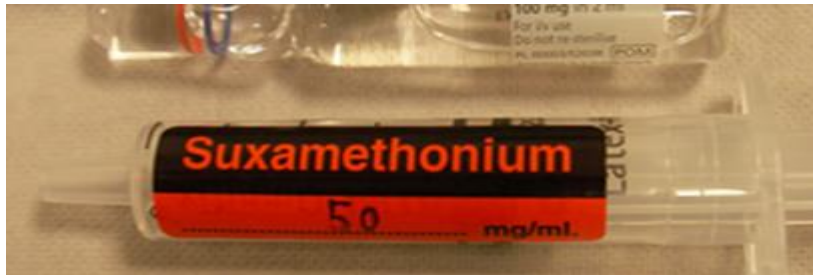
DIAGNOSE NOW!

Pharmacological dangers and problems

Myotonic Dystrophy

Suxamethonium can induce masseterspasm and/or generalized muscle rigidity making;

- Intubation impossible
- Ventilation difficult or impossible



WARNING

Pharmacological dangers and problems II

Myotonic dystrophy

- Can be extremely sensitive for respiratory depressant effects in drugs especially opioids.
- Caused by;
 - Lower sensitivity for $p\text{CO}_2$ in CNS respiratory centre
 - Peripheral muscle weakness



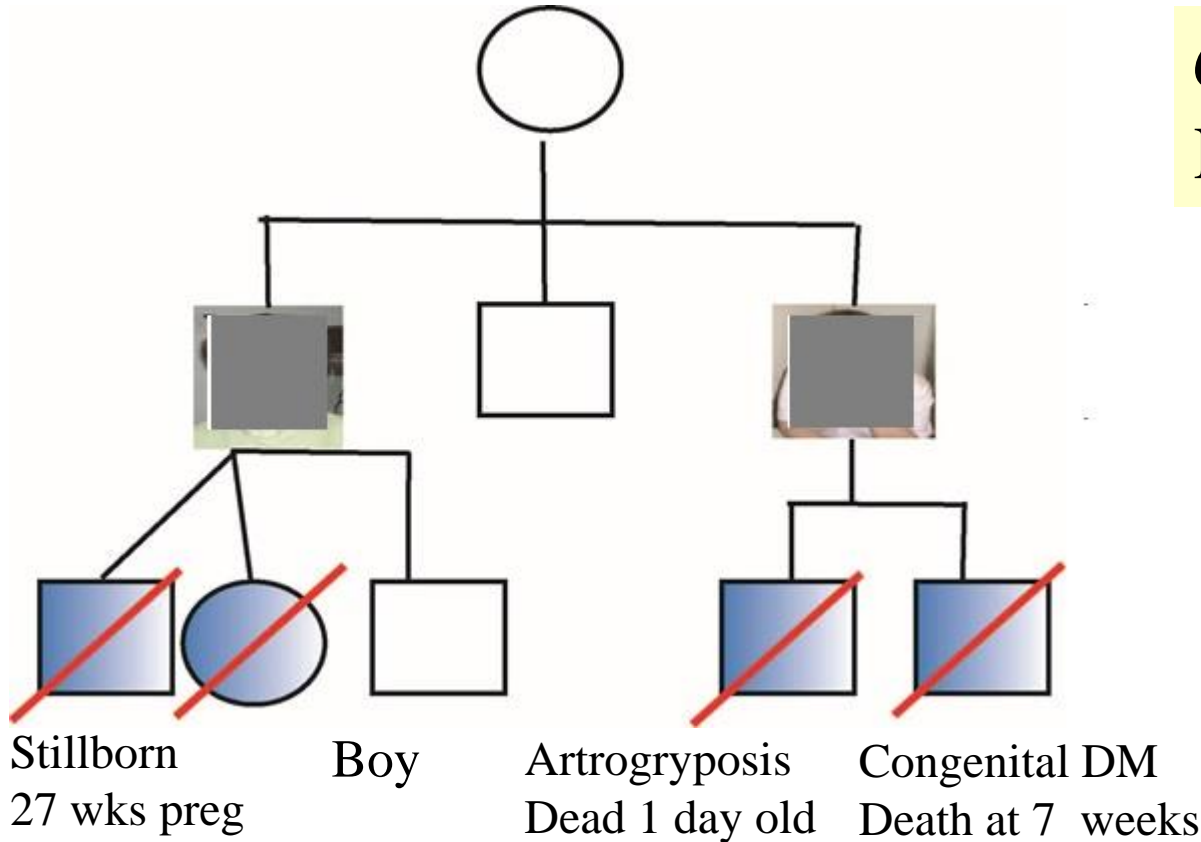
WARNING
Be vigilant



Obstetrics & Diagnostics

Eur J Obstet Gynecol Reprod Biol. 2004 May 10;114(1):44-53. Rudnik-Schöneborn Zerres K

To make a diagnose backwards



Generation 1
Prematur cataract

Generation 2
"Classical"
Myotonic dystrophy

Generation 3
Congenital
Myotonic dystrophy

If general anaesthesia is necessary – how I would do?

- **Be prepared – Be vigilant (always..)**
- **Do not give suxamethonium**
- **RSI with large dose of rocuronium**
- **Shortacting opioids**
- **Reverse with sugammadex**
- **Sevo/Iso/Des/N₂O is OK**

Congenital myotonias

- Congenital myotonia
 - Thomsens myotonia
 - Beckers myotonia
- **Only myotonic symptoms**
- **No other organ manifestations**
- **Pure chloride channel disease**

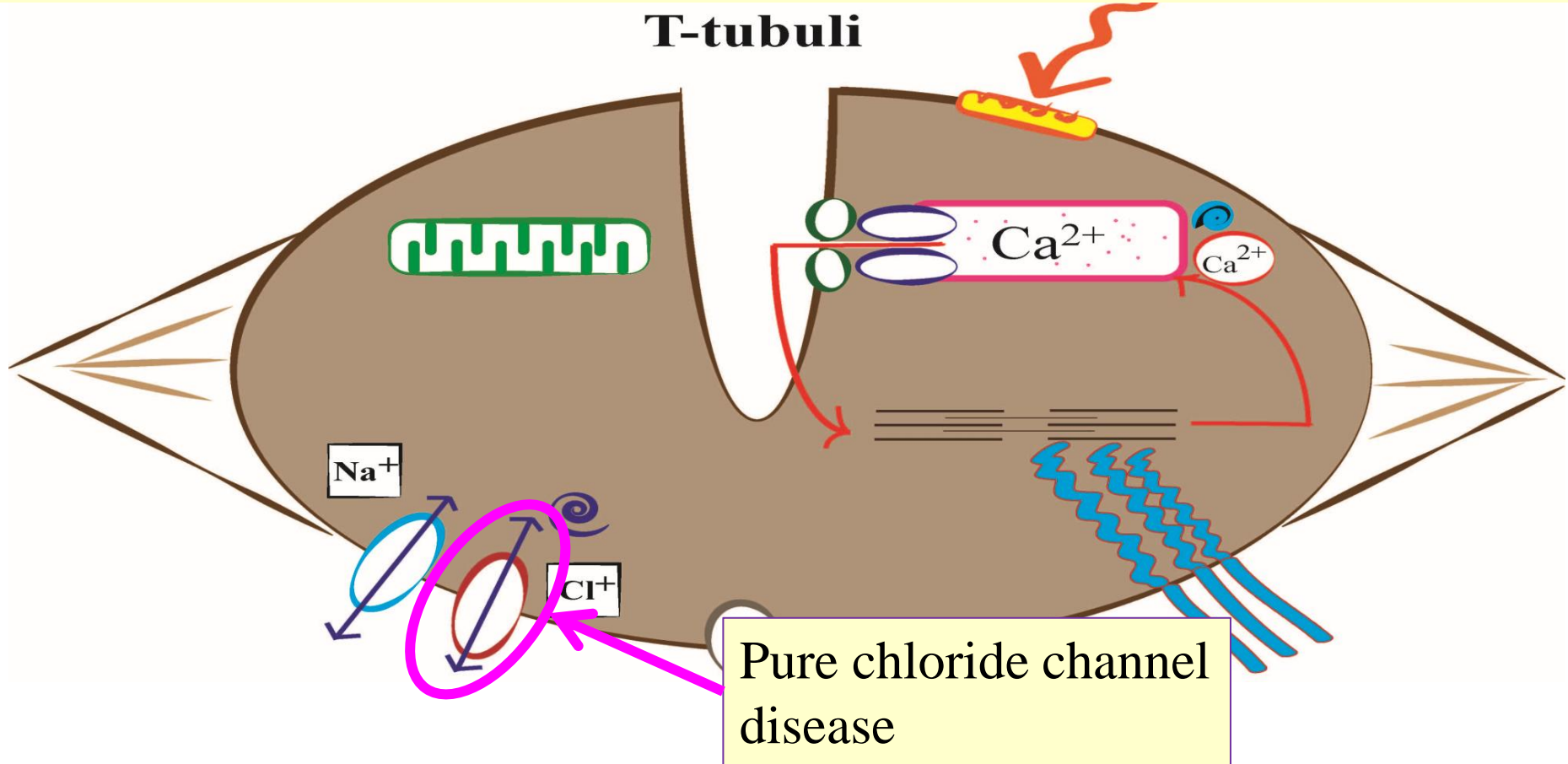
Risk:

Myotonic reaction – can preclude ventilation

Suxamethonium induced masseterspasm

Patophysiology

T-tubuli



What can induce myotonia during anaesthesia?

Suxamethonium



Do not give suxamethonium

Shivering/
hypothermia



Keep patient warm
Monitor core temperature

Rough surgeon



”Elegant surgeon”

Diathermy/electro-
cautery



Bipolar preferably
If monopolar beware of the plate.

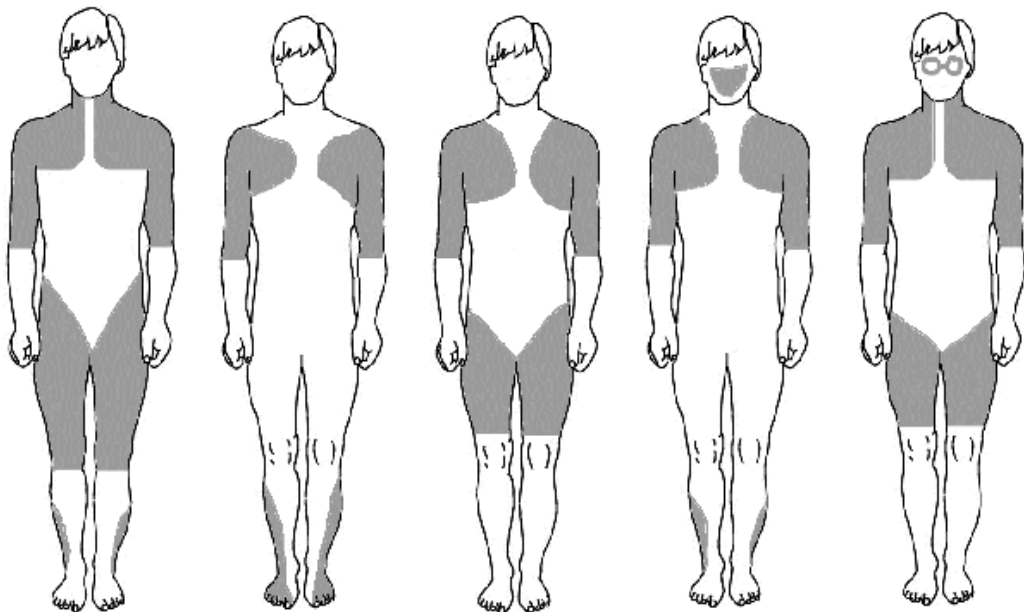
Reverseral



Use rocuronium and reverse with
sugammadex.

Muscle dystrophies

Breakdown of muscles over time



Duchenne and
Becker Types

Emery-Dreifuss
Type

Limb Girdle
Type

Facioscapulo-
humeral Type

Oculopharyngeal
Type

MUSKELDYSTROPHIES

- **Duchennes och Beckers muskeldystrophy** *DMD*
- **Limb Girdle Muscle Dystrophy** *LGMD*
- **Emery-Dreifuss Muscle Dystrophy** *EDMD*
- **FacioScapuloHumeral Muscle Dystrophy** *FSHMD*
- Welanders myopathy
- Etc.

Mb Duchennes DMD

- Mothers are mutation carriers
- **Sons** (~50%) have the disease

It can be good to know

Duchenne carriers (always women) can have cardiomyopathy and sometimes weak skeletal muscles.

Limb Girdle Muscle Dystrophy LGMD

Many different genes **Variation in symptoms**

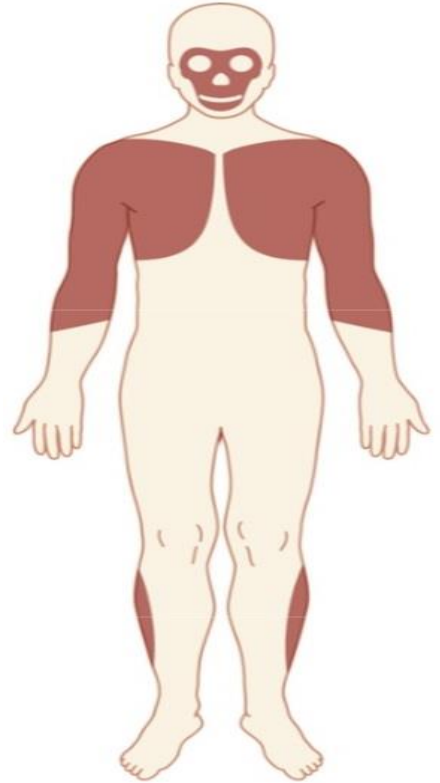
- Cardiac failure (even leading transplantation)
- Respiratory failure upto ventilator dependent
- Muscle weakness, contractures
- Very little symptoms....



Limb Girdle MD

FacioSkapuloHumeral MuscelDystrophy

FSMD Landouzy-Dejerines sjukdom



Emery-Dreyfuss Muscle Dystrophy *EDMD*

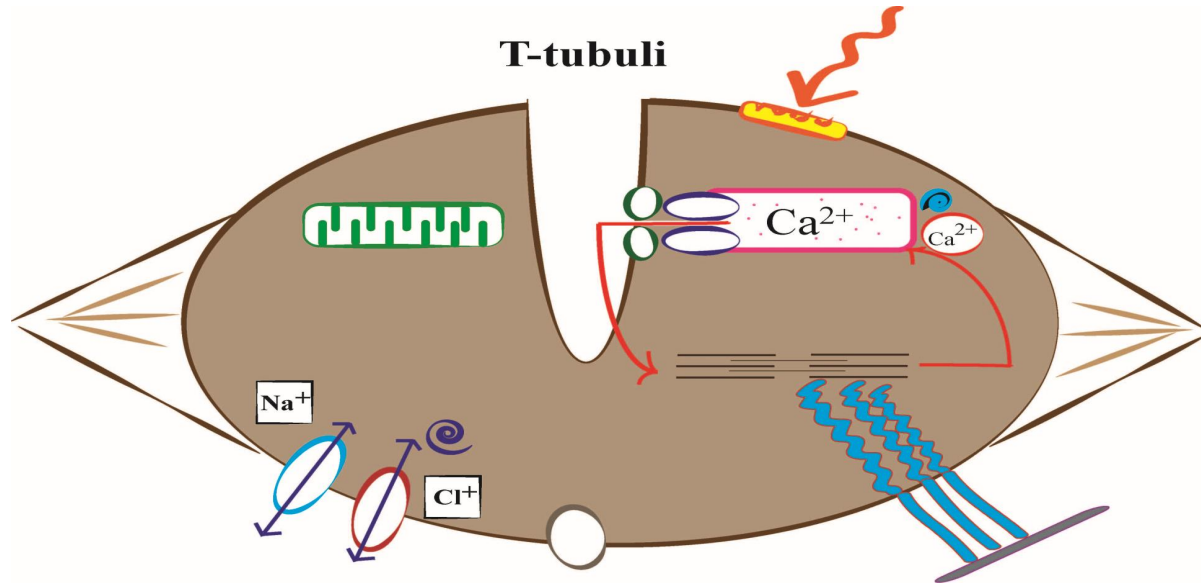
Very Rare

- **Cardiomyopathy**
- Arrhythmias
- Often ICD/pacemaker

Periodic paralyses

It is what it sounds like

- Hyperkalaemic Periodic Paralysis **HyperPP**
- Hypokalaemic Periodic Paralysis **HypoPP**



MH

What is MH????

Whats wrong?

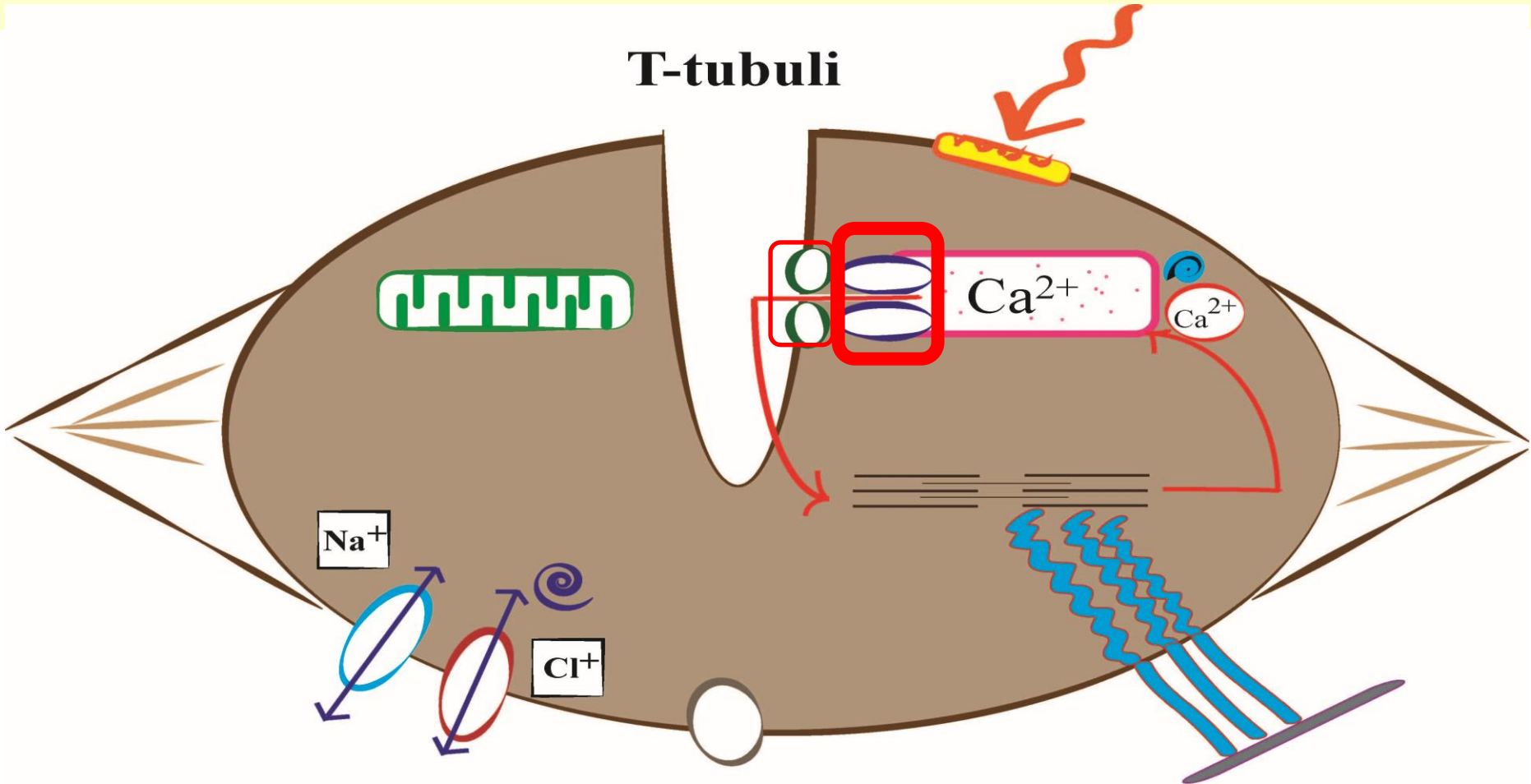
Impaired intracellular Ca^{2+} homeostasis

Triggering agents:

- Halogenated inhalational anaesthetics
 - Sevo/Des/Iso
- Suxamethonium

MH pathophysiology

T-tubuli



Ca²⁺

Hyperkalemia
Myoglobinuria
H⁺
Etc.

Leaky cell membrane

Anaerob metabolism

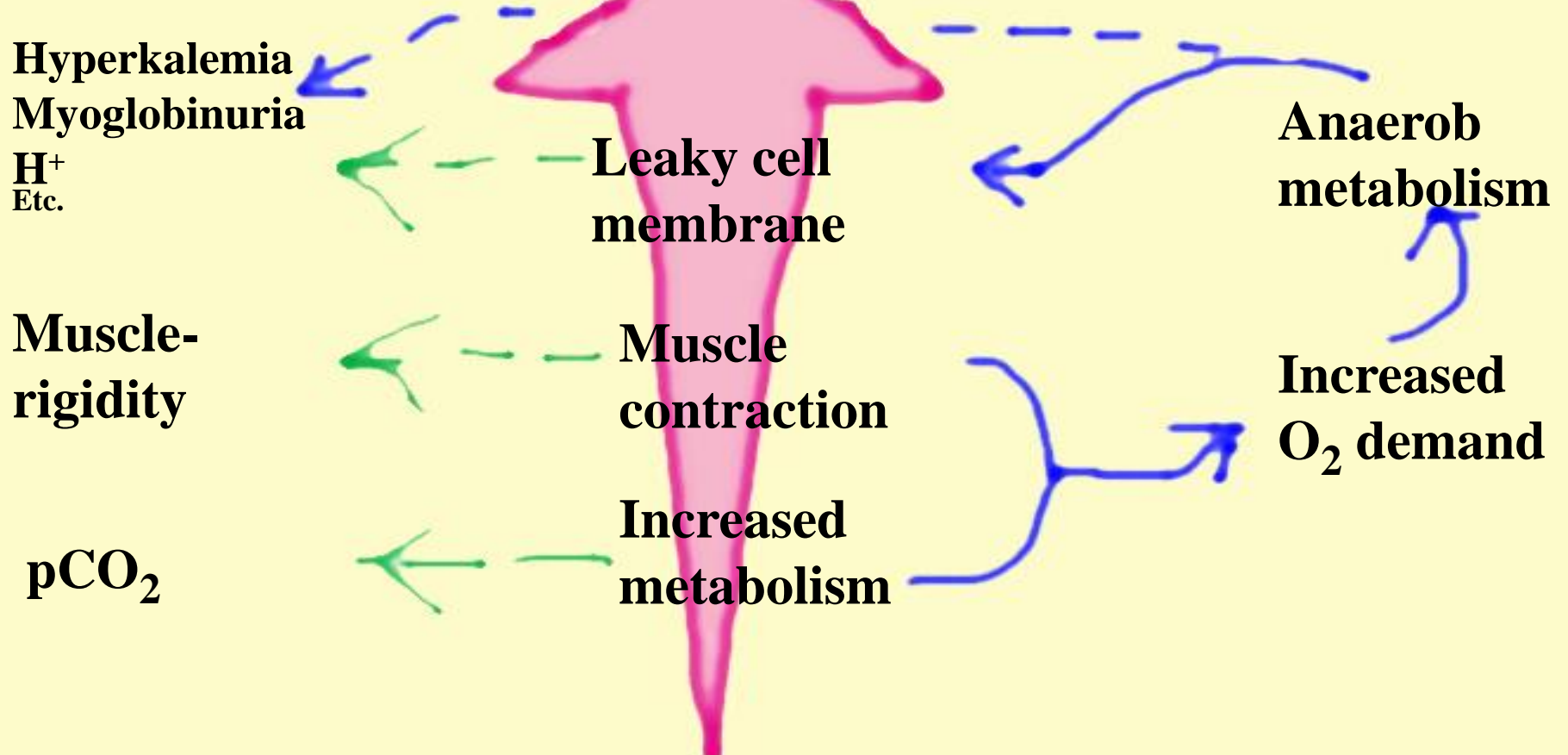
Muscle-rigidity

Muscle contraction

Increased O₂ demand

pCO₂

Increased metabolism



Mortality

Mortality

Sweden 3 in 30 years

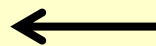
Literature reports <5%

However

USA

In hospital 7%

Office based 21 %



WHY?

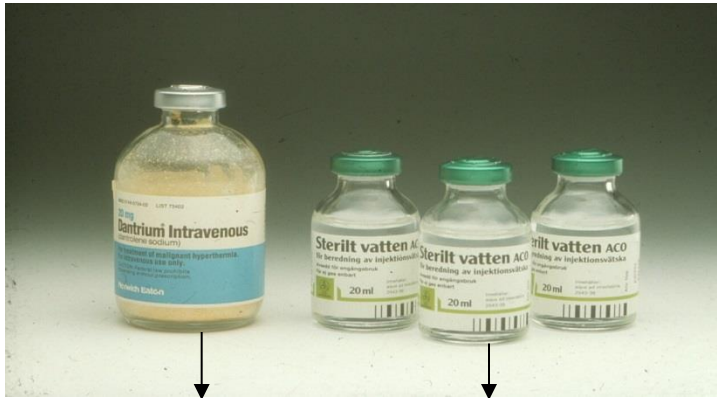
My personal thoughts:

More "in office" anaesthesia in USA. A fulminant MH reaction requires a lot of staff. Not always available in office.

I have experienced 3 real fulminant cases. We were 9 staff working on all 3 occasions.

Treatment Dantrolen

MOST important



20 mg dantrolen
3 g mannitol

60 ml
Sterile water

0,33 mg/ml

- **Initial dose 2,0 mg/kg**
- Call for people it will be needed
- 1 bottle á 20 mg contains 3 g mannitol
- Use room temperature sterile water

Diagnoetics

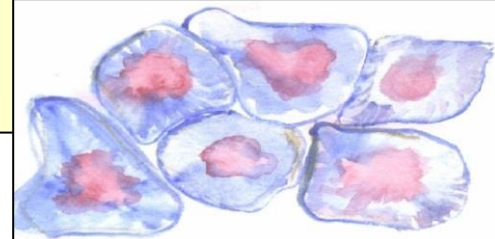
What answer can you get from?

- **IVCT In Vitro Contracture Test ??**
 - **Establishing diagnosis**
 - **Rouling out diagnosis**
- **Mutation analysis ??**
 - **Establishing diagnosis**
 - **Cannot rule out MH susceptibility**

Diseases linked to MH (known today) (but not necessarily "the same as")

- **Central Core Disease CCD**
 - Rule of thumb; all muscle disease with core in the name. Control
- King Denborough syndrome
- Hypo Kalaemic Periodic Paralysis (*hypoKPP*)
- Excertional Heat Stroke

CCD
Histopathology



MH Masseter spasm and CS

- **Masseter spasm** (MMS) =
Jaws of steel for at least 2 minutes

Masseterspasm and caesarean section

GA+MMS+CS can be sign of

- **MH**
- **Myotonic disease** (suxamethonium induced myotonic reaction)
- **Stress** your internal watch is running very fast
- **Extreme but normal** phenomena

Congenital myopathies
A quite new field
Not much knowledge yet

Congenital myopathies: not only a paediatric topic.

H Jungbluth Kings College London

- Nemaline myopathy
- Central core disease (CCD) we know connection to MH
- Multiminicore Disease (MmD)
- And many others

MITOCHONDRIAL DISEASES

Intuitively it is felt like very rare

Prevalence – 1/4000

One single mutation has prevalence of 1/500

....A bit confusing

Names some examples

- **MELAS** **Mitochondrial Encephalomyopathy with Lactic Acidosis and Stroke-like episodes**
- **Leighs disease**
- **MERRF** **Myoclonic Epilepsy with Ragged-Red Fibers**
- **Kern-Sayers**
- **MNGIE** **Mitokondrial NeuroGastroIntestinal Encefalomyopati**

Mitochondrial disease

Summary of pathophysiology

- **Batteries not included or not charged enough**
- **No/small metabolic reserves**
- Diagnose can be difficult with no signs in daily life
- Stress can be life threatening



Mitochondrial disease labour Risks

Pregnancy is usually, but not always, well tolerated

- Increased risk for **preeclampsia**
- Risk for **Mg²⁺ toxicity** even with therapeutic concentrations. **Vigilance!**
- Increased risk for **gestational diabetes**
- Increased risk for **preterm delivery**

Mitokondriesjukdom

Pregnancy NewCastle Guidelines

All women with mitochondrial disease shall have

- Early obstetric assessment
- Close monitoring throughout pregnancy
- Access to specialist multi-disciplinary care
- Links with fetal medicine

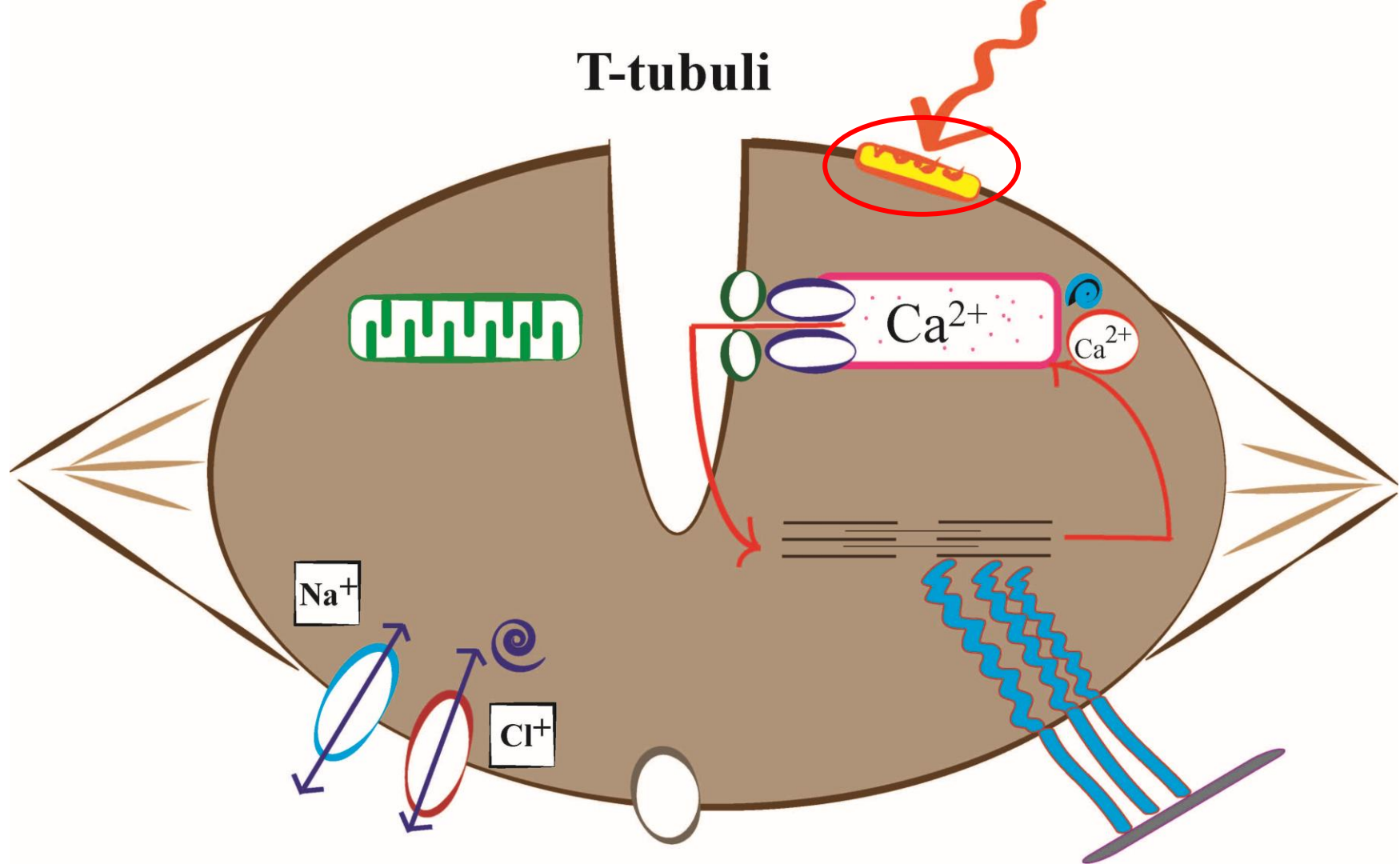
Mitochondrial disease and labour

How I would think

- Planning and vigilance
- Pregnancy is a metabolic load
 - No energy deficiency – give glucose with electrolytes
- Fever Infection and acidosis should be treated "aggressively"
- Normothermia. Prevent shivering

MYASTHENIA GRAVIS

T-tubuli

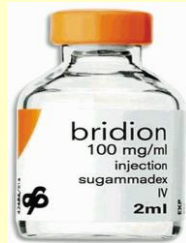


Myasthenia gravis & pregnancy

- Myasthenias gravis prevalence in pregnancies is 1/20 000.
- Myasthenic crisis can be lethal.
- Material from USA 1991
 - 4% mother mortality
 - 5 times increased neonatal baby mortality
 - Babies get transplacental transfer of ACh antibodies from their mothers

Myasthenia gravis and CS

- **Spinal often best - as usual.**
- If compromised breathing, general anesthesia could be better. Individualise.
- Potent inhalational anesthetics are OK
- Relaxation two choices:
 - **Suxamethonium** Give 1,5- 2 times normal dose (=150-200mg)
 - Myasthenia Gravis is no contraindication for suxamethonium
 - **Rocuron** Give a incremental low dose and
 - reverse with **sugammadex**.



All types of anaesthetics have been used with both success or failure

Pharmacological dangers and problems

- **Mg²⁺ can induce muscle weakness. Deaths reported.**
- **Hypokalaemia** can worsen symptoms
- **Drugs that can worsen symptoms**
 - Aminoglykosides
 - Linkosamines
 - Fluorokinolon,
 - Gabapentin

Case myasthenia gravis

- Woman 38 y. Treated for MG
- Spinal
- **Post partum day 2. Extremely rapid development of respiratory failure. Cardiac arrest. Resuscitated**
- Ventilator antibiotics pyridostigmin azathioprin and steroids
- Leave ICU after 5 days
- Healthy baby

Charcot Marie Tooth CMT

- Progressive deteriorating muscle atrophy due to neuropathy.

CS Spinal most probably best.

Millers textbook ed. 2015 is

**warning for neurological
deterioation after spinal**

Careful positioning

Pharmacological dangers and problems

Charcot Marie Tooth

- **Thiopentone**
 - Increased sensitivity related to seriousness of disease
- **Furadantine** and perhaps fluorokinoles are contraindicated due to risk for deterioration of neuropathy

Spinal muscle atrophy SMA

Spinal Muscle Atrophy

- Recessive inherited disease
 - Symptoms from neonatal death to normal life span
-
- They can be extremely difficult/impossible to intubate
 - Epidural or spinal can be difficult/impossible
- In the same patient**

All known anaesthesia techniques and intubation techniques have been used with result; success as well as catastrophe

Spinal Muscle Atrofi SMA

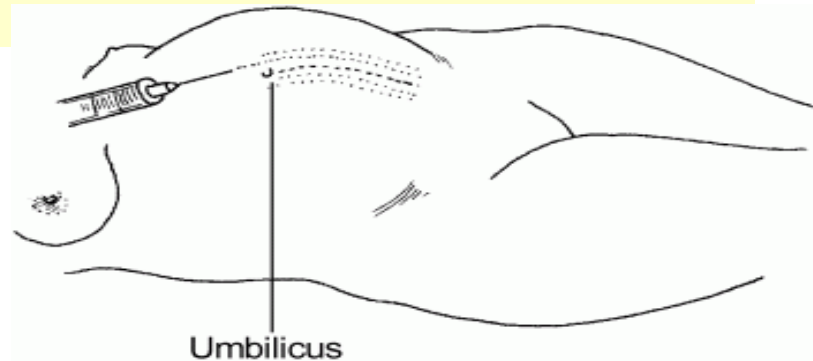
- Pregnancies are not uncommon
- Increased risk for
 - Preterm delivery 30% (Σ^{***}),
 - CS or instrumental delivery > 60% (Σ^{***})
- Anaesthesia could be a total night mare.

Do not forget the possibility of cesarean
in infiltration anaesthesia.

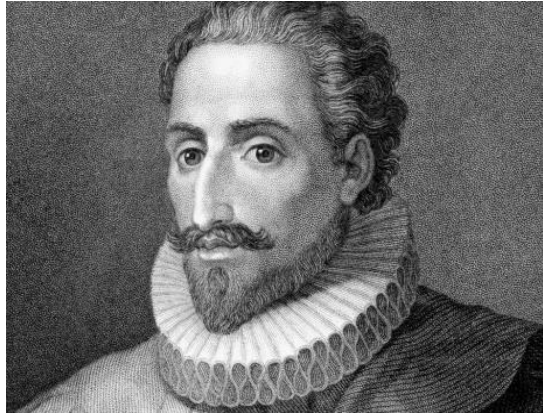
To be provocative

- **Every anaesthesiologist should be able to do a surgical airway**
- **Every obstetrician should be able to perform a cesarean in infiltration anaesthesia????**

Informative instructions on WHO's website.



How to think



Cervantes 1547-1616

*”To be prepared is
half the victory”*