Mitochondrial Disorders and Anesthetic Implications

Allison Kinder Ross, MD
Professor and Chief,
Division of Pediatric Anesthesia
Duke University Medical Center

No disclosures related to topic or agents discussed.

On May 11, 2012, at 4:31 PM, "Kirk Lalwani" <lalwanik@ohsu.edu> wrote:

> Hi Allison,
>
> Hope all is well with you.
>
> As you may be aware, I'm the program Chair for the 2013 Winter SPA meeting. Our theme is Childhood Obesity and the meeting kicks off with 3 talks on Obesity.
>
> I would like to invite you to participate in our other offerings. Based on your previous work, we would be grateful if you could give a Refresher Course Lecture on 'Pathophysiology and Anesthetic Management of Mitochondrial Diseases In Children'.
>
> I'd be very grateful for your participation. Please let me know if you are available to present. I look forward to hearing from you.
>
> Thanks,
> Kirk
>
> Kirk Lalwani, MD, FRCA, MCR
> Associate Professor of Anesthesiology and Pediatrics,
> Director, Pediatric Anesthesiology Fellowship Program,
> Oregon Health and Science University,

How did I get here???

On May 11, 2012, at 6:42 PM, "Allison Ross, M.D." <allison.ross@duke.edu> wrote:

> Hi, Kirk.
> I have heard wonderful feedback as to your work within the SPA. Congratulations.
> I appreciate the offer to speak on this important subject but do not feel qualified as I have no research in this field. Did you try Phil Morgan? If you exhaust other options, I can fill in.
> Is this in Vegas?
> Allison

Did you try Phil Morgan?

CHIEF COMPLAINT: Bacteremia.

HISTORY OF PRESENT ILLNESS: This is a 6-year-old white male with a past medical history significant for mitochondrial disease and complete TPN dependency, who previously presented to this hospital on 8/16/05 with complaints of lethargy and not feeling well. At that time, the patient was admitted to the hospital and his TPN regimen was adjusted on the belief that his symptoms were the result of inadequate volume. During the course of that admission, blood cultures were drawn in the ER and shortly after the patient was discharged home it was discovered that one of his blood cultures was positive for what eventually proved to be coagulase-negative staphylococci. The patient was brought back to the hospital on that evening and started on IV vancomycin. After IV vancomycin therapy was well established, the patient was again discharged home after again further blood cultures had been drawn. The decision was made to do this because the patient has an excellent home health establishment and it was not thought to be a problem to treat the patient with four weeks of vancomycin IV at home. On the date of discharge, the patient had another positive blood culture which was known to be gram-negative rods. When the speciations on this returned, the infection was discovered to be Bacillus cereus and the patient was again contacted at the beginning of this week and asked to return to the hospital for removal of his internal jugular Hickman catheter and replacement of his central venous access in vascular radiology. The patient was admitted to the hospital at 10 p.m. in the evening on 8/23/05 in order for this procedure to be done as soon as possible.

PHYSICAL EXAMINATION: Temperature 36.9, pulse 90, respirations 18, blood pressure 87/50. General appearance of the patient: No apparent distress. Skin/mucosa: Skin was intact without visible rashes, erythema, or lesions. Mucosa was moist with no signs of inflammation. There was no swelling, redness, or tenderness. Head and neck: Neck was supple. There were no enlarged lymph nodes. Chest/back: The Hickman port site on the patient's right upper

no signs of cyanosis. The patient presented with a normal gross neurological exam with no focal or gross abnormalities served.

HOSPITAL COURSE: On the morning after admission, anesthesiology was contacted at 7 a.m. to see if a slot could be arranged for the patient's line to be changed out later in the day. The patient is known to have allergies to all anesthetic gases and after extensive conversation with anesthesia, it became clear that the appropriate personnel would not likely be available for this procedure until the following morning. At that time, the patient's mother stated that she would like to leave the hospital and return the next day to have the procedure done as an outpatient. Dr. Woods spent much time expressing her concerns for the patient leaving and detailed with great specificity the reasons for the patient to stay in house overnight, including concerns about worsening bacteremia from the source of a line infection. The patient's mother again stated her desire to leave and return with the patient in the morning. Therefore, the patient was scheduled for changing out of his line in the morning and was discharged home.

www.UMDF.org


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MITOCHONDRIAL
DISEASE
FOUNDATION®
HOPE. ENERGY. LIFE.

Pediatric Anesthesia 2007 **17**: 1–6 doi:10.1111/j.1460-9592.2006.02106.x

Editorial

Muscular dystrophy versus mitochondrial myopathy: the dilemma of the undiagnosed hypotonic child

ALLISON KINDER ROSS MD

Division of Pediatric Anesthesia, Duke University Medical Center, Durham, NC, USA

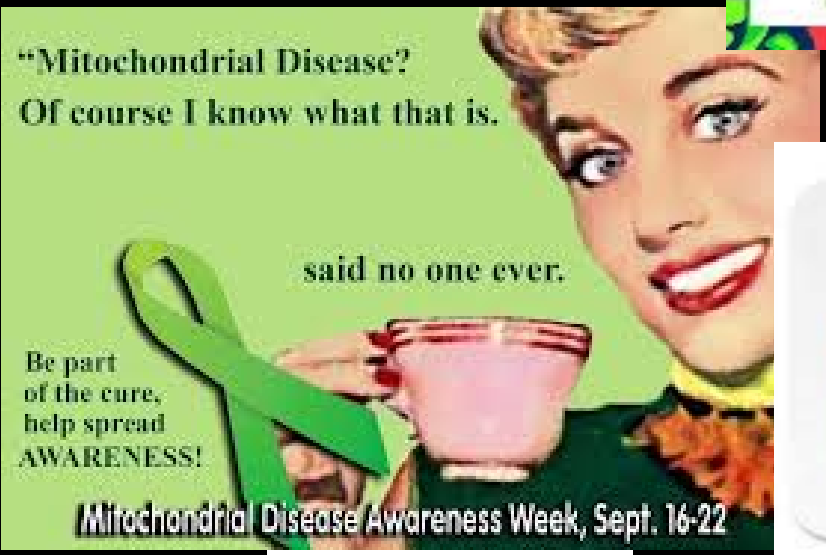
Mitochondrial Disorders
Mitochondrial Diseases

- Minimal risk of 1 in 4000
- Mitochondrial myopathies account for most common cause of muscle weakness in children.


Swat Out
Mitochondrial Disease


the mito murfee scarf
bundle up in the perfect fall accessory
As the weather gets chilly, what better way to stay warm than in our limited edition Mito Murfee Scarf - designed exclusively for In The Pink by Lilly Pulitzer. 100% of all proceeds will benefit MitoAction, the nonprofit working to improve the quality of life for patients living with Mito, a disease for which there is no cure.
Get wrapped up in this wonderful cause today!
mitoACTION
in the pink


BULLY
Mitochondrial Disease


"Mitochondrial Disease?
Of course I know what that is.
said no one ever.
Be part of the cure, help spread AWARENESS!
Mitochondrial Disease Awareness Week, Sept. 16-22

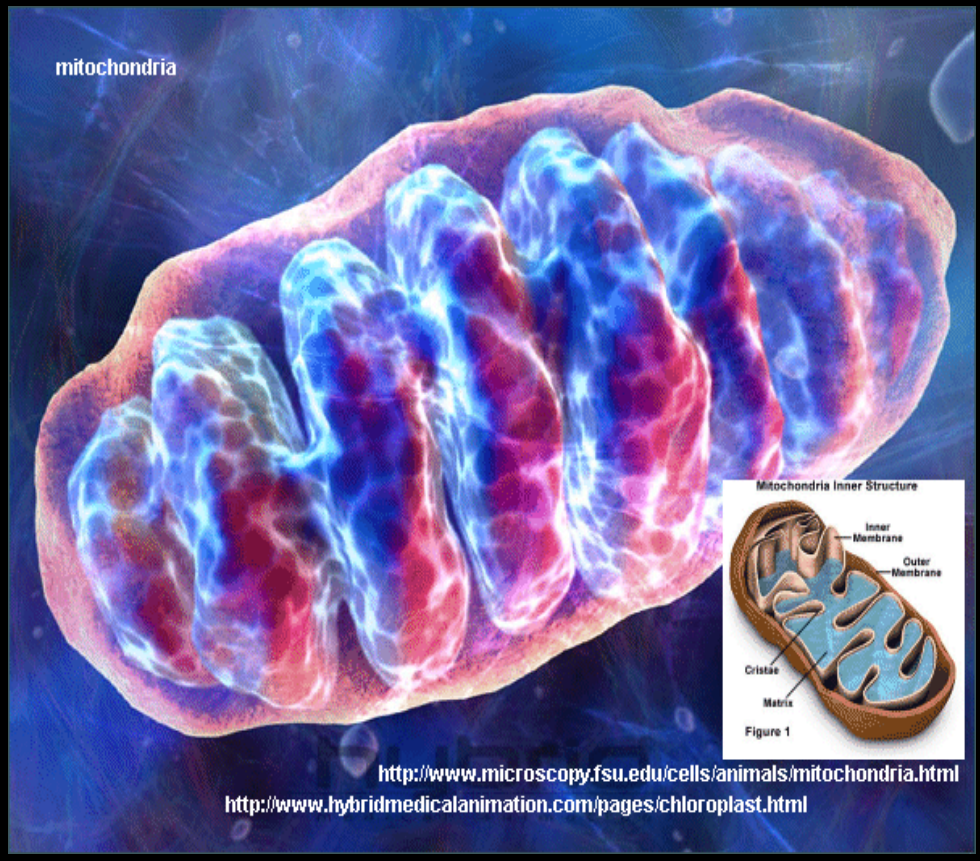

STAMP OUT
Mitochondrial Disease

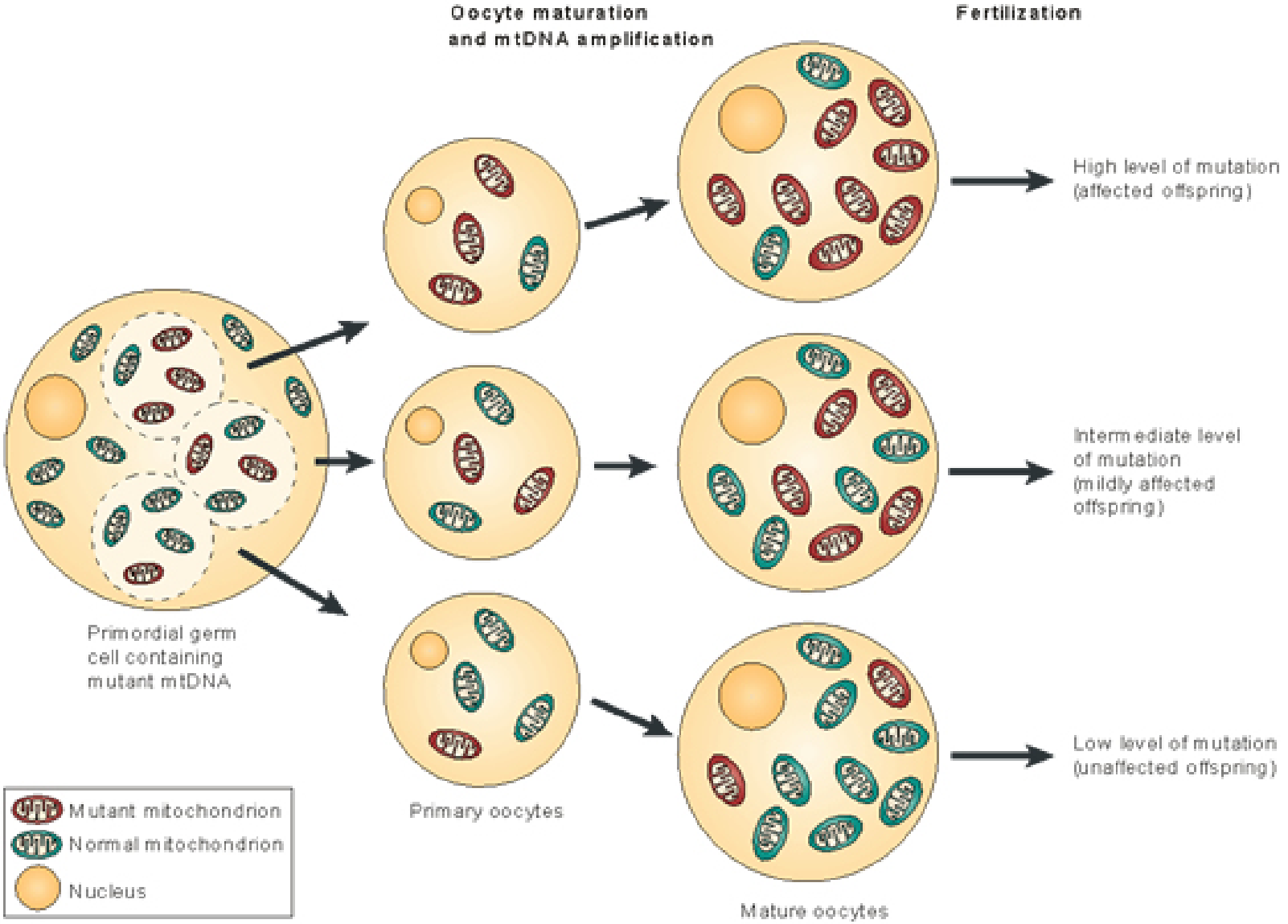

Awareness Week
September 18–24, 2011
What is Mitochondrial Disease?
UNITED MITOCHONDRIAL DISEASE FOUNDATION
Learn more www.umdf.org
HOPE

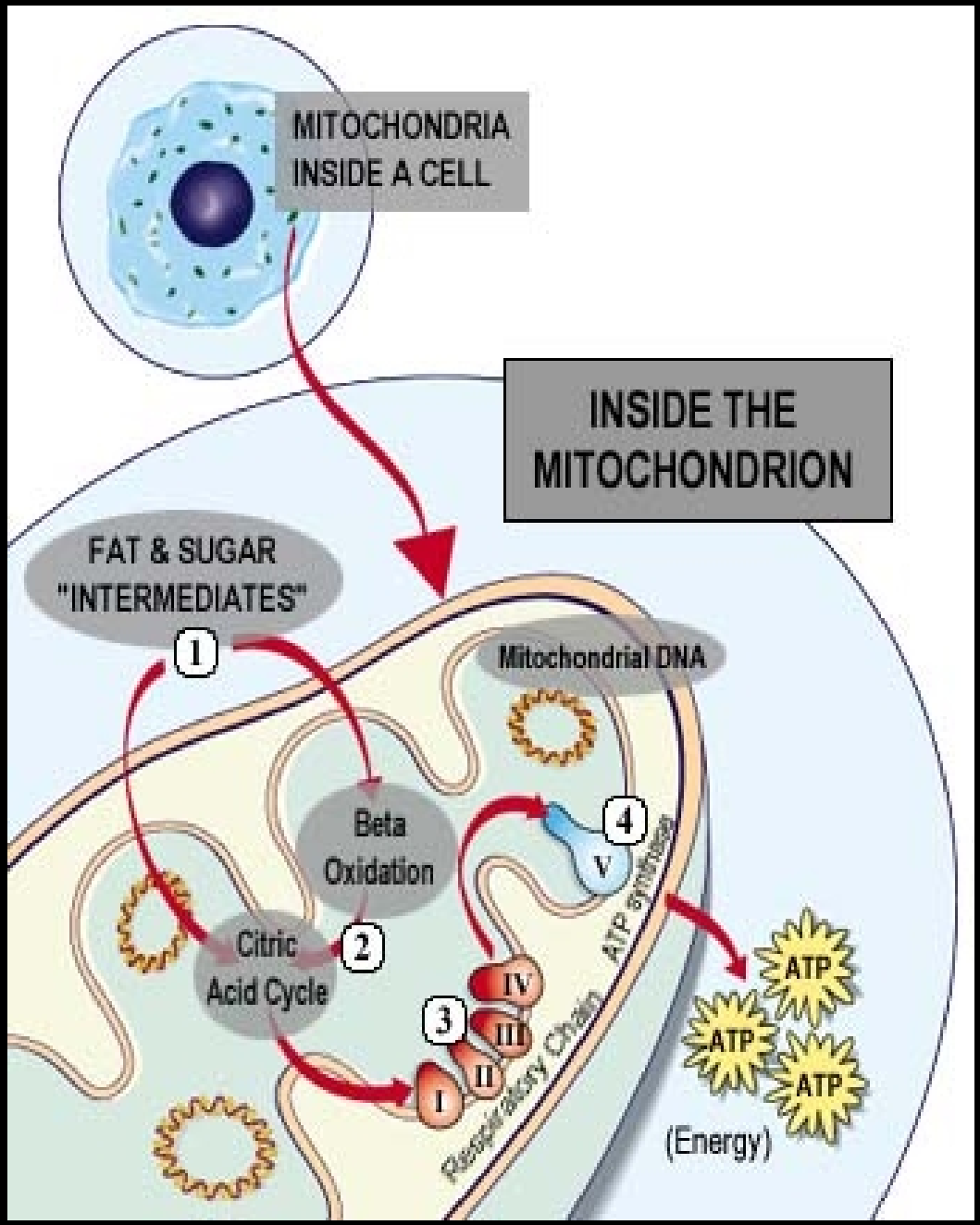

Buck
Mitochondrial Disease

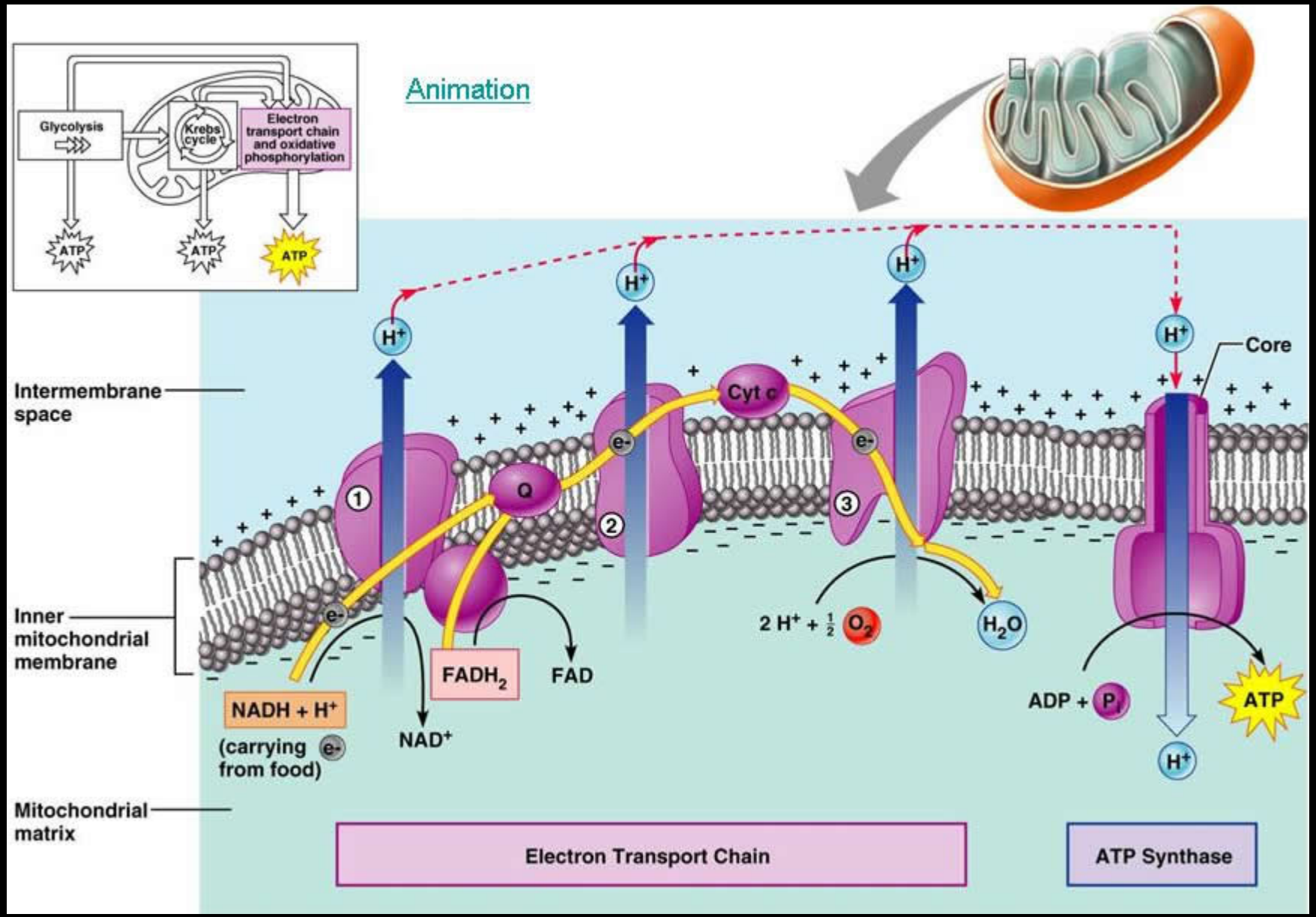
Mitochondria

- Found in all cells (except RBCs)
- Possess their own DNA, unique from other DNA
  - Maternal inheritance
- Primary function
  - Energy (ATP) Production
    - Oxidative phosphorylation
    - Electron transfer chain




Oocyte maturation
and mtDNA amplification
Fertilization
High level of mutation
(affected offspring)
Intermediate level
of mutation
(mildly affected
offspring)
Low level of mutation
(unaffected offspring)
Primordial germ
cell containing
mutant mtDNA
Primary oocytes
Mature oocytes
Mutant mitochondrion
Normal mitochondrion
Nucleus


MITOCHONDRIA
INSIDE A CELL
INSIDE THE
MITOCHONDRION
FAT & SUGAR
"INTERMEDIATES"
1
Mitochondrial DNA
Beta
Oxidation
Citric
Acid Cycle
2
3
4
V
IV
III
II
I
Respiratory Chain
ATP synthase
ATP
ATP
ATP
(Energy)



http://classes.midlandstech.edu

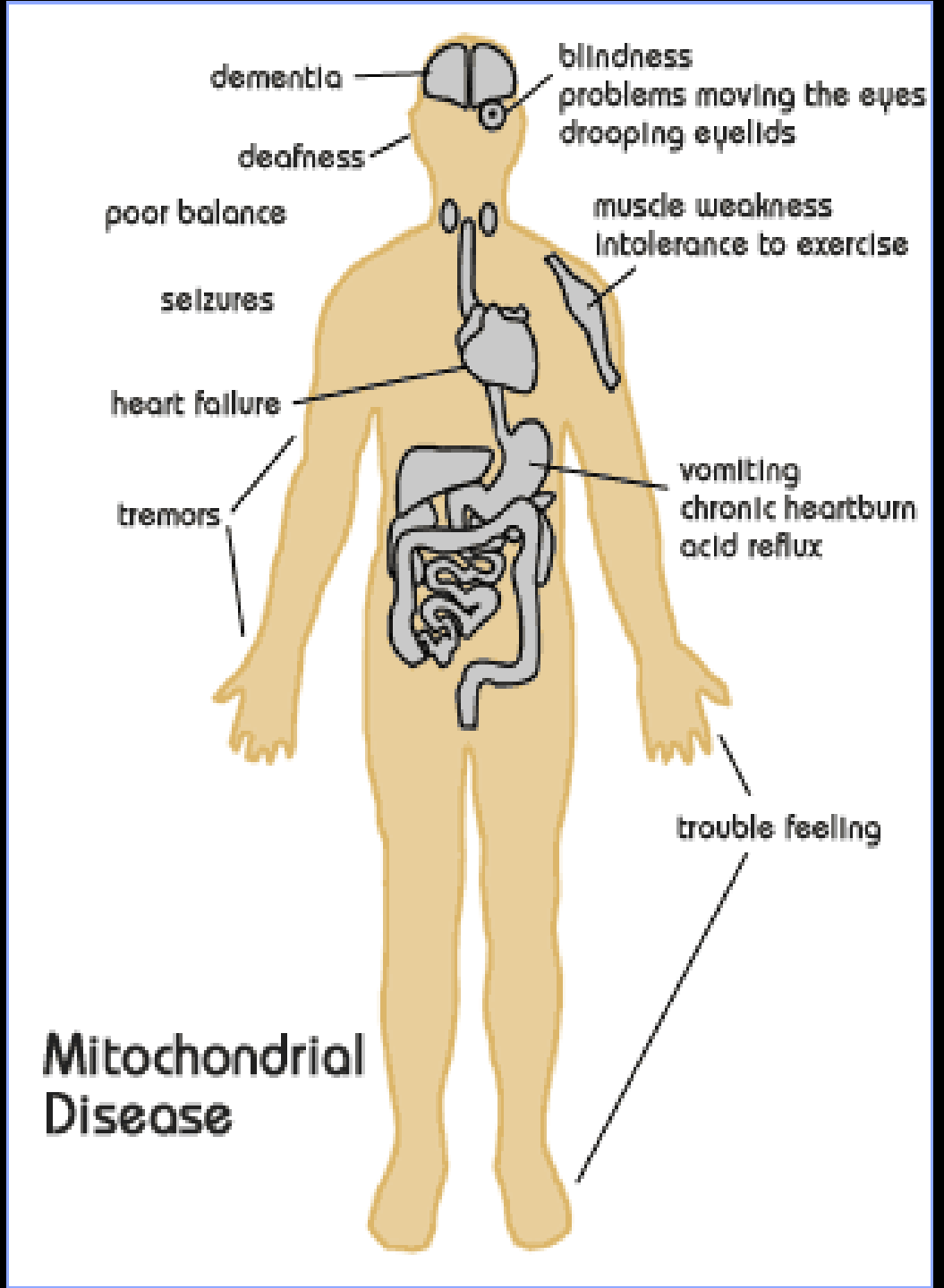
Mitochondrial Disorders and Clinical Features

DISORDER	CLINICAL FEATURES	Additional Features
Alpers-Huttenlocher syndrome	Hypotonia Seizures Liver failure	Renal tubulopathy
Chronic progressive external ophthalmoplegia (CPEO)	External ophthalmoplegia Bilateral ptosis	Mild proximal myopathy
Kearns-Sayre syndrome (KSS)	PEO Pigmentary retinopathy One of the following: CSF protein> 1g/L, cerebellar ataxia, heart block	Bilateral deafness Myopathy Dysphagia Diabetes mellitus Hypoparathyroidism Dementia
Infantile myopathy and lactic acidosis	Hypotonia in first year of life Feeding and respiratory difficulties	Fatal form may be associated with cardiomyopathy and/or Toni'Fanconi-Debre syndrome
Leber hereditary optic neuropathy (LHON)	Subacute painless bilateral visual failure Males:females 4:1 Median age of onset 24 years	Dystonia Cardiac pre-excitation syndromes
Leigh syndrome (LS)	Subacute relapsing encephalopathy Cerebellar and brainstem signs Infantile onset	Basil ganglia lucencies Maternal history of neurologic disease or Leigh syndrome
Mitochondrial encephalopathy with lactic acidosis and stroke-like episodes (MELAS)	Stroke-like episodes Seizures and/or dementia Ragged red fibors and/or lactic acidosis	Diabetes mellitus Cardiomyopathy Bilateral deafness Pigmentary retinopathy Cerebellar ataxia
Myoclonic epilepsy myopathy sensory ataxia (MEMSA)	Myopathy Seizures Cerebellar ataxia	Dementia Peripheral neuropathy Spasticity
Myoclonic epilepsy with ragged-red fibers	Myoclonus Seizures Cerebellar ataxia Myopathy	Dementia Optic atrophy Bilateral deafness Peripheral neuropathy Spasticity Multiple lipomata
Neurogenic weakness with ataxia and retinitis pigmentosa (NARP)	Late childhood or adult-onset peripheral neuropathy Ataxia Pigmentary retinopathy	Basal ganglia lucencies Abnormal electoretinogram Sensorimotor neuropathy
Pearson syndrome	Sideroblastic anemia of childhood Pancytopenia Exocrine pancreatic failure	Renal tubular defects

Modified from Chinnery. Mito Gene Review, 2010

Mitochondrial Disease and Multisystem Involvement

- Nervous
- Muscular
- Renal
- Cardiovascular
- Respiratory
- Hepatobiliary
- Gastrointestinal



Anesthetic Management of Children with Mitochondrial Disease

- Preoperative evaluation
- Preoperative preparation
- Intraoperative management
- Postoperative disposition

Preoperative Evaluation in Mitochondrial Disease

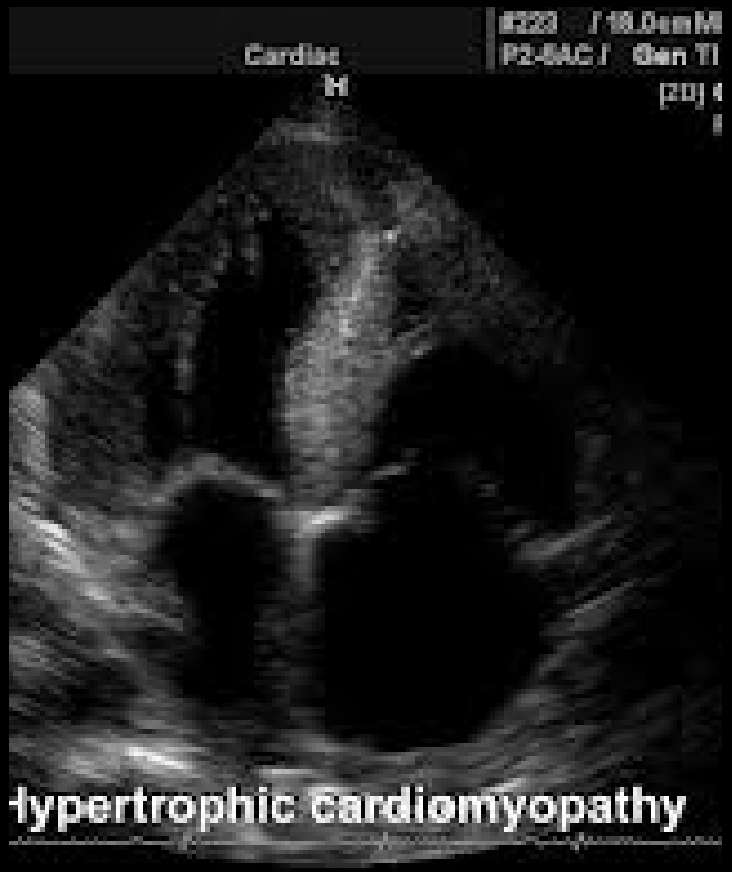
- History
  - Associated conditions
- Physical exam
- Laboratories
- Diagnostic studies

Laboratory Values

- Electrolytes, LFTs
  - Looking for renal, hepatic dysfunction
- Lactate
  - Elevation is nonspecific
  - NOT ALL PATIENTS WITH MITOCHONDRIAL DISEASE WILL HAVE ELEVATED LACTATE LEVELS
  - Fasting blood lactate >3 mm/L suggests MD
  - A lactate/pyruvate ratio > 20 suggests disorder in oxidative phosphorylation
- Creatine Kinase
  - Typically normal or slightly elevated
  - Depends on muscle involvement

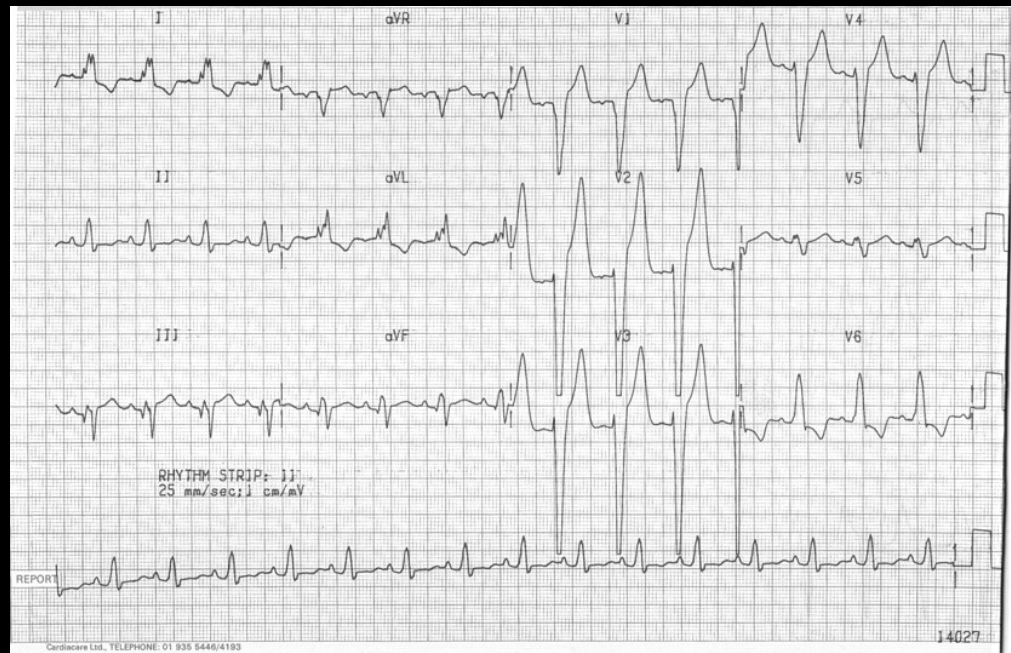
Diagnostic Procedures

- Respiratory
- Cardiac
  - EKG
  - ECHO
- Neuro
  - ?MRI



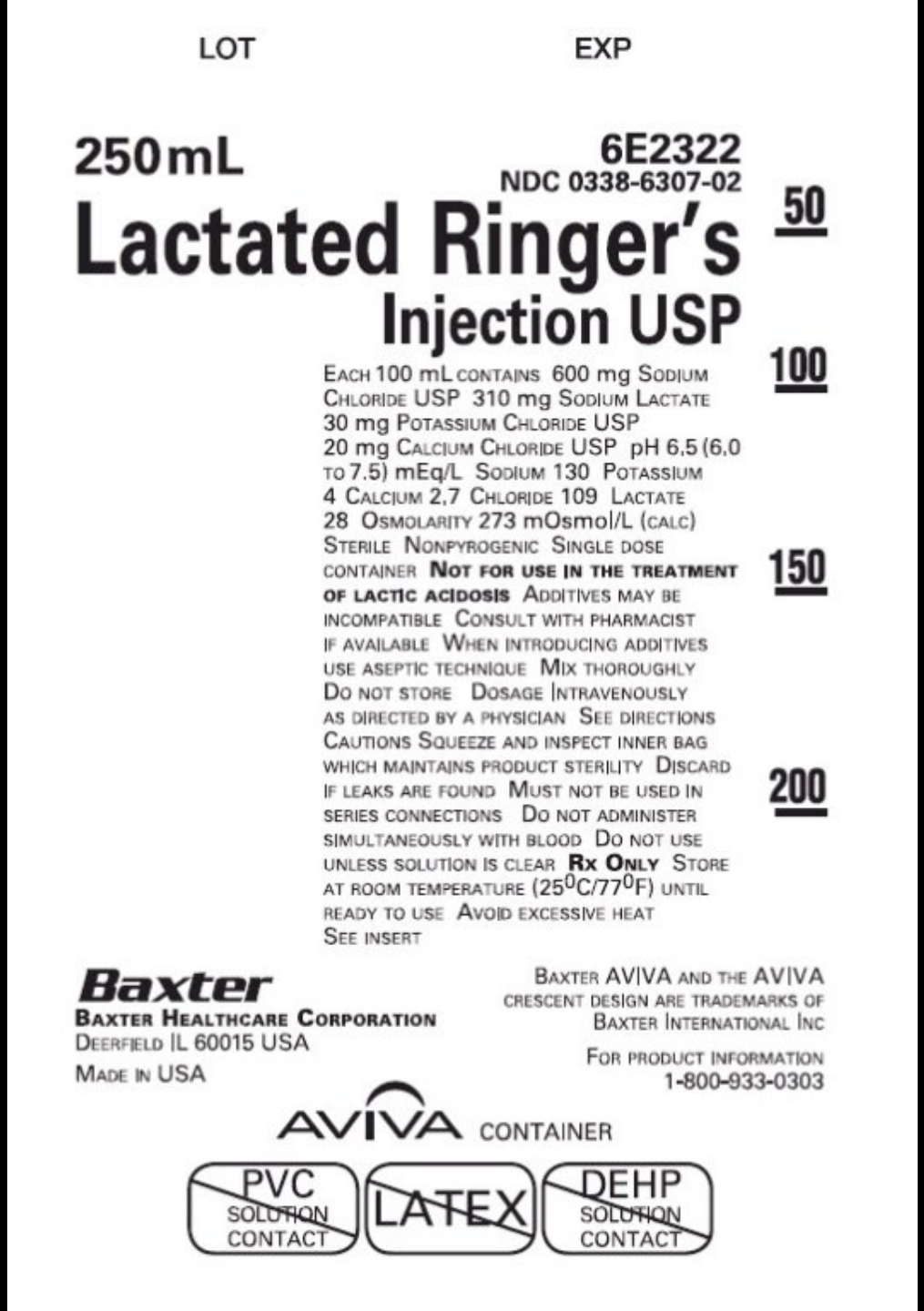
Preoperative CV Workup

- Mito patients are at higher risk for
  - Dilated and hypertrophic cardiomyopathies
  - Pre-excitation syndromes
  - Conduction blocks
  - Hypertension
  - Sudden death



Preoperative Preparation

- Minimize preop fasting period
- Liberal glucose-containing clear fluids up until 2 hours prior to procedure
- Intravenous glucose-containing solution once NPO
  - Avoid lactate-containing solutions (no LR)

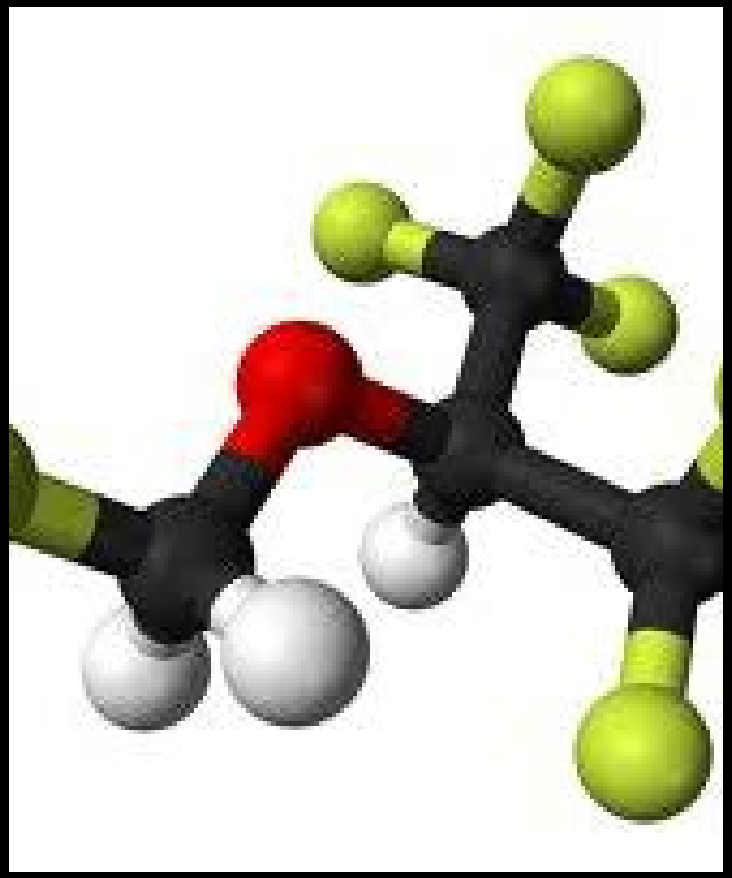


I liter Lactated Ringer's
Contains Sodium Lactate
Lactate = 28 mEq/L

Sodium lactate metabolism to bicarbonate "depends on oxidative cellular activity"

Anesthetic Management

- Volatile agents
- Intravenous agents
- Muscle relaxants
- Opioids
- Regional anesthesia



DIVISION OF MEDICAL GENETICS
EMERGENCY METABOLIC PROTOCOL

To Whom It May Concern:

This letter regards a patient of the Metabolic Clinic at Duke University Medical Center, [redacted] He might have a mitochondrial disorder, based upon his clinical presentation and the lack of confirmatory testing to date. A muscle biopsy is planned for further evaluation. In the interim, the following are some general guidelines for his care.

General considerations for care

Certain drugs are known to be toxic for patients with a mitochondrial disorder. Specific drugs to avoid include the following: valproate, barbiturates, tetracyclines, chloramphenicol, and aminoglycosides (gentamicin). Erythromycin also might not be well tolerated. Avoid nitrous oxide at the dentist. ~~Precautions during general anesthesia include those for malignant hyperthermia risk.~~

Table 1

Table 1. Sensitivity of 16 Children with Mitochondrial Defects to Sevoflurane

Patient No.	Age (yr)	Procedure	% Sevoflurane (BIS = 60)	Diagnosis
1	1	Skin biopsy, line placement	0.4	**Leigh disease**
2	3	Herniorraphy	3.0	Complex III
3	5	Herniorraphy	3.1	Complex III
4	1	Muscle biopsy	**0.8**	**Complex I**
5	2	Muscle biopsy	3.1	No complex identified
6	5	Muscle biopsy	3.2	Complex III
7	1	Muscle biopsy	3.5	No complex identified
8	3	Muscle biopsy	4.0	No complex identified
9	2	Muscle biopsy	3.2	No complex identified
10	1	Muscle biopsy	2.9	No complex identified
11	2	Muscle biopsy	3.4	No complex identified
12	1	Muscle biopsy	**1.6**	**Decreased pyruvate oxidation**
13	4	Muscle biopsy	**1.0**	**Decreased glutamate oxidation**
14	2	Muscle biopsy	3.1	Complex III
15	10	Muscle biopsy	3.5	Complex III
16	5	Muscle biopsy	3.0	Complex III

BIS = Bispectral Index.

ANESTHESIOLOGY

Mitochondrial Defects and Anesthetic Sensitivity

Morgan, Phil G.; Hoppel, Charles L.; Sedensky, Margaret M.

Anesthesiology. 96(5):1268-1270, May 2002

Table 1. Sensitivity of 16 Children with Mitochondrial Defects to SevofluraneBIS = Bispectral Index.

Inhaled Agents

- Abnormal halothane-caffeine contracture test
  - 66 yo for hernia
  - Test requested by anesthesiologist
  - 4 prior GAs without issue
  - Hernia with nontriggering agents

- "Mitochondrial diseases may be associated with an abnormal halothane caffeine contracture test." and "It cannot be ruled out that MH-like manifestations may develop…"
  - Finsterer. Metabolic Brain Disease, 2009

Risk of Malignant Hyperthermia in Undiagnosed Hypotonic Children

- True relationship exists with only two disorders
  - King's Syndrome
  - Central Core Disease

Rhabdomyolysis

- Risk depends on degree of myopathy
- Clinically and pathophysiologically distinct entity from MH
- Can result in hyperkalemic arrest
- Myoglobinuria may be early sign

Intravenous Anesthetics

- Propofol
- Etomidate
- Thiopental
- Ketamine
- Dexmedetomidine

- Although children with mitochondrial disorders have increased sensitivity to these agents, all intravenous induction agents have been used safely and effectively in children with mitochondrial disorders.

Risk Factors for Development of Propofol Infusion Syndrome

- Young age
- Dose >4 mg/kg/hr
- Duration of >48 hours
- Underlying illness (respiratory or neurologic)
- Concomitant catecholamine or steroid

Mitochondrial Disease and Propofol Infusion Syndrome

- Mitochondrial dysfunction is underlying mechanism
  - Propofol diffuses easily across membranes
    - Lipophilic nature and small molecular weight
    - Intracellular mitochondrial binding
    - In vivo experiments show direct impairment of mitochondrial function
      - Inhibits electron flow along electron transport chain
      - Lower ATP production
      - Induces uncoupling and inhibition of Complexes I and II
      - Increased acylcarnitine concentrations

Metabolic Acidosis due to Propofol Infusion

Farag, Ehab M.D., F.R.C.A.; DeBoer, Glenn M.D.; Cohen, Bruce H. M.D.; Niezgoda, Julie M.D.

Anesthesiology . 102(3):697-698, March 2005.

As a referral center for mitochondrial diseases, we use the muscle biopsy as one tool for assisting in the diagnosis of mitochondrial disorders. We avoid the use of propofol for anesthetizing patients undergoing this procedure. In the past, we have used short-term (15–30 min) and low-dose infusions of propofol for noninvasive diagnostic procedures in known mitochondrial patients. However, we have found in the more symptomatic patients that the use of propofol has been associated with prolonged anesthesia recovery and at times required intensive care unit admission. It seems that the duration of the infusion and the total dose of propofol may be the critical factors in these cases. In addition to propofol inhibiting mitochondrial metabolism, the lipid component of the formulation may play a role in toxicity for

Mitochondrial Disease and Propofol Another Issue…

- Propofol infusion given for status epilepticus.
- Multiorgan system failure.
- Muscle biopsy inconclusive due to fatty infiltration of sample.
- Returns to OR months later for definitive biopsy with “allergy to propofol”.

Public Opinion of Propofol

- “It therefore seems likely that patients with mitochondrial defects may be at seriously increased risk from this drug.” *www.pedsanesthesia.org/meetings/2007winter/pdfs/Morgan-Friday1130-1150am.pdf*
- ”Has been shown to impair mitochondrial function to a greater degree than other anesthetics. Adverse events with other induction agents such as ketamine, thiopental and etidomate have not been reported to date.” *www.umdf.org*

Alternatives to Propofol

- Thiopental
- Ketamine
  - Analgesic properties may be beneficial
- Etomidate
  - Effect of adrenal suppression
- Dexmedetomidine

Summary of IV Agents

- All agents have been used with success in patients with mitochondrial disorders
- Propofol clearly has effects at the mitochondrial level, although clinical relevance is unclear at normal anesthetic doses
- There are alternatives to propofol that have not been associated with adverse outcomes

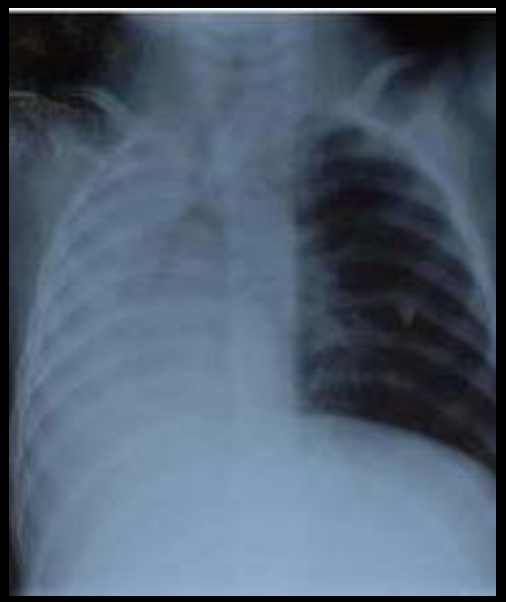
Neuromuscular Blocking Agents

- Possible decreased clearance
  - Hepatic involvement
  - Renal involvement
- Consider atracurium
- Increased sensitivity questioned
  - Depends on degree of myopathy
  - Depends on concomitant use of antileptics
- All muscle relaxants have been used safely and effectively, but must be used in moderation and with close TOF monitoring.


1000 mg TOTAL

Opioids

- All have been used and with variable reports.
- Risk of respiratory insufficiency
- Use sparingly and consider postop ventilation



Local/Regional Anesthesia

Pros

- May reduce requirements of other agents
- May improve postop respiratory status

Cons

- Children often have peripheral neuropathy
- Effects of local anesthetics at cellular level?

Anesthesiology. 2007 May;106(5):1026-34.

Effects of intermittent femoral nerve injections of bupivacaine, levobupivacaine, and ropivacaine on mitochondrial energy metabolism and intracellular calcium homeostasis in rat psoas muscle.

Nouette-Gaulain K, Sirvent P, Canal-Raffin M, Morau D, Malgat M, Molimard M, Mercier J, Lacampagne A, Sztark F, Capdevila X.

- Results: Adenosine triphosphate synthesis and adenosine triphosphate-to-oxygen ratio were significantly decreased in the muscle of rats treated with local anesthetics. A global decrease (around 50%) in all of the enzyme activities of the respiratory chain was observed.

Postoperative Management

- Special attention to glucose stability, temperature, and respiratory parameters
- Mild disease, minor noninvasive procedure, no complications
  - Observation in recovery area
- Moderate-severe disease, other procedures, with or without complications
  - Overnight or greater observation
  - Monitored setting for many children with mitochondrial disorders

Anesthesia-related morbidity and mortality after surgery for muscle biopsy in children with mitochondrial defects. Driessen et al. Ped Anes 2007

- Data from 122 children <10 years (mean age 32.4 mos) for muscle biopsy
- Preoperative evaluation
  - Encephalopathy in 93
  - Muscle weakness in 32
  - Lactic acidosis in 15
  - Cardiomyopathy or conduction defects in 10
  - Chronic respiratory problems in 7

Driessen et al. Ped Anes 2007

- Anesthetic plan at discretion of anesthesiologist
  - Mask inductions and IV inductions
  - Dextrose infusions in all
  - Maintenance mostly with inhaled agents, few propofol
  - Most mask cases
  - No NMB, one sux
  - Wounds infiltrated with bupivacaine
- No major anesthetic-related complications in children with mito for muscle biopsy

The risk of malignant hyperthermia in children undergoing muscle bopsy for suspected neuromuscular disorder. Flick et al. Ped Anesth 2007

- 274 children for muscle bx
  - All exposed to volatile
  - 3 received sux
- Results
  - None with s/sx MH or rhabdomyolysis
    - Zero CCD or King syndrome
    - 7 muscular dystrophy (2 DMD)
    - 3 confirmed mitochondrial disorder
- Conclusion/Thoughts
  - Only CCD and King syndrome clearly linked
  - Risk of developing MH or rhabdomyolysis 1.09%

Mitochondrial disease and general anesthesia: a case series and review. Footitt et al. BJA 2008

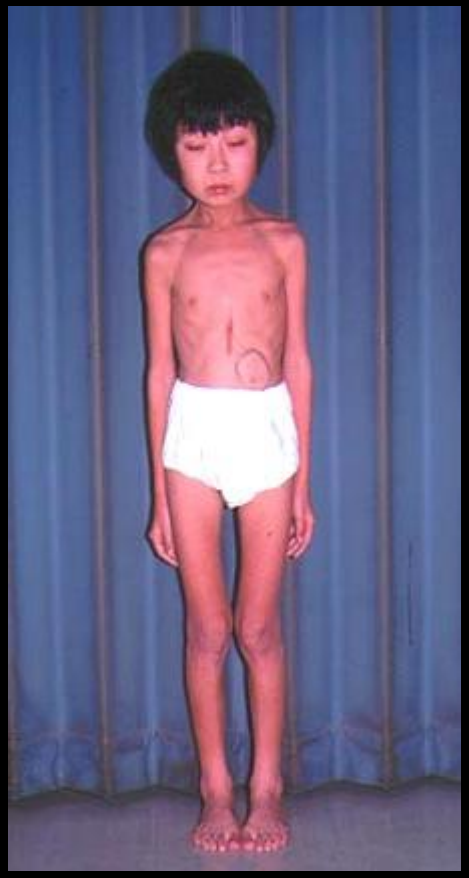
- 38 mito patients for 58 procedures under GA
  - Mean age 4 years
  - Median duration 1 hour
  - Variety of IV and inhaled agents, NMBs (2 sux), analgesics
  - Most had dextrose infusions and prior to procedure
  - No episodes MH or rhabdomyolysis
    - 1 patient with respiratory failure, acidosis 24 hours postop---?etiology? Presumed Leigh's

Intraoperative Management Generalizations

- Avoid increased energy production
  - Normothermia
  - Pain-free
  - No acidosis
- Avoid decreased energy supply
  - Shortened NPO period
  - Provide glucose
  - PONV prophylaxis
  - Euvolemia

Kearns-Sayre Syndrome

- Slowly progressive mitochondrial DNA deletion disorder
- Triad of features:
  - Onset before age 20
  - Progressive, external ophthalmoplegia
  - Pigmentary degeneration of retina
- Cardiac conduction defects

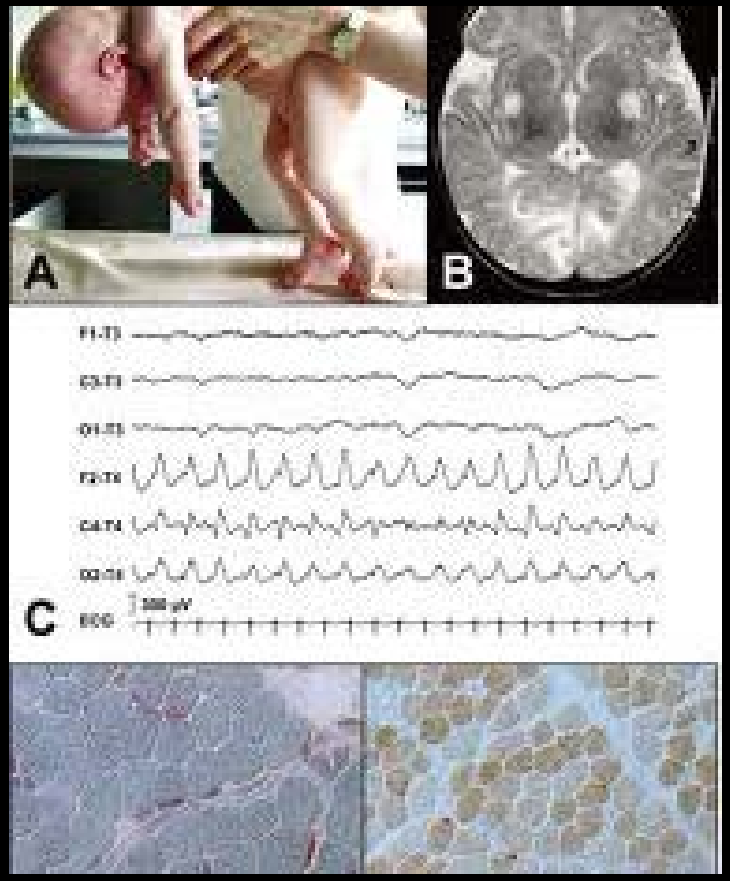


Intraop Management of Child with Kearns-Sayre Syndrome

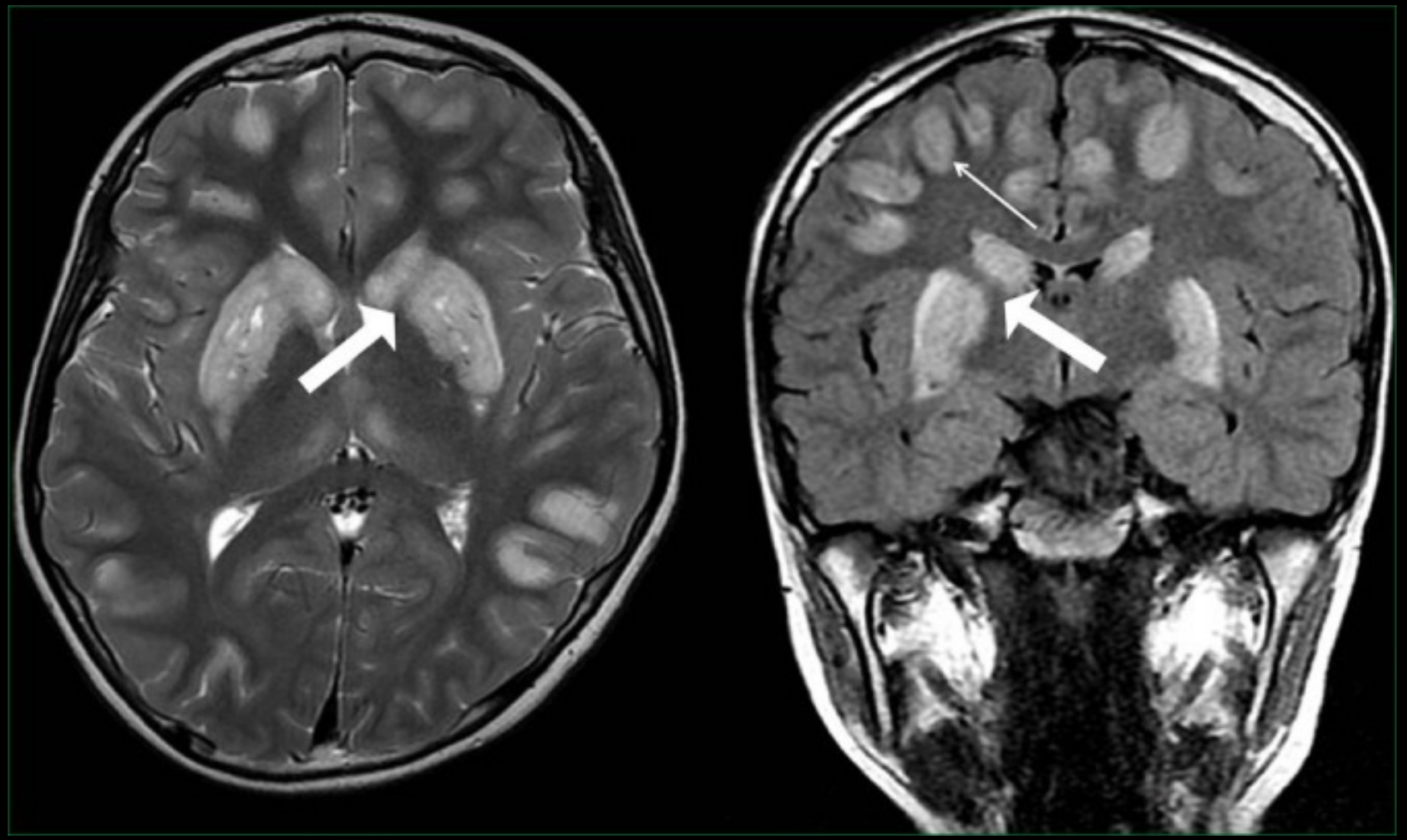
- Unique anesthetic management geared towards AV-conduction block
  - Increased risk of dysrhythmias
  - Have external pacing capability
  - Have isoproterenol infusion in room

Leigh Syndrome

- Subacute necrotizing encephalomyelopathy
- Fatal disease
- Diagnosis
  - MRI/CT
  - neuropathological exam
- General anesthetics highly risky, particularly in the presence of respiratory symptoms



trialx.com



Saudi J Anaesth. 2012 Apr-Jun; 6(2): 181–185.

Author / year	Age / gender	Surgical procedure	Induction of anesthesia	Maintenance of anesthesia and intraoperative fluids	Perioperative outcome and issues
Ward[7], 1981	14.5 month old / F	Surgical correction of strabismus and myringotomy tube		Halothane	Marked development milestone regression
Greenberg *et al.*,[14] 1990	10 month old / M 5.5 year old / F	Lumbar puncture evoked potential examination CT scan	Sedation with oral chloral hydrate (100 mg / kg)		Respiratory failure (both patients)
Grattan-Smith *et al.*,[15] 1990	M	Pneumo-encephalogram	Thiopental sodium, suxamethonium	Halothane and nitrous oxide	All three patients developed respiratory failure. All had preoperative respiratory manifestations
	M	Muscle biopsy	Thiopental	Thiopental	
	F	Bronchoscopy		Halothane	
Shenkman *et al.*,[16] 1997	5 month old / F	Extracorporeal shockwave lithotripsy	Ketamine, midazolam	Propofol and N_2O 70% D5 ½ NS	None
Cooper *et al.*,[17] 2003	21 years / F	Scoliosis surgery	Midazolam, propofol , fentanyl, vecuronium	Maintenance anesthesia no specified. Ringer's lactate	Acute lung injury, sepsis, respiratory failure, reactivation of her brain disease, then died
Shear *et al.*[10], 2004	19 month old / F	Muscle biopsy	Glycopyrrolate, ketamine	Spinal anesthesia with tetracaine	None
Jacobs *et al.*,[18] 2004	17 years / F	Scoliosis surgery	Sevoflurane (8%) in O_2 / N_2O (70% / 30%)	Propofol (150-200 µg / kg / minute), remifentanil , cisatracurium propacetamol, tramadol, morphine. Crystalloids included Plasmalyte and tetrastarch	None
Ellis *et al.*,[19] 2005	16 years / F	Molar extraction	Midazolam and propofol	Propofol infusion	Intraoperative seizures
Gozal *et al*,[20] 2006	6 year / F 2 year / F 1.5 year / M 0.5 year / M 3 year / F	Percutaneous endoscopic gastrostomy	Propofol	Propofol infusion (50–100 µg / kg / min)	None
Sasaki *et al*,[21] 2008	17 years / F	Laryngotracheal separation and open fundo-plication	Vecuronium	Propofol (75–100 µg / kg / minute) and fentanyl infusions	None. Mechanical ventilation and propofol sedation continued for seven days postoperatively to prevent the surgical stress response
Our case	15 years / M	Dental rehabilitation	Propofol, fentanyl	Propofol infusion, cisatracurum, fentanyl, paracetamol, and diclofenac. Normal saline 9%	None

Saudi J Anaesth. 2012 Apr-Jun; 6(2): 181–185.

Keys to Anesthesia for Mitochondrial Disease

Thorough preop workup.

Do not increase energy requirements.

Provide supplemental energy supply.

UMDF Website

Table 1. Metabolic stressors that can lead to decompensation in patients with mitochondrial disease

Stressor	Suggested action
fasting	Perform surgery first thing in the morning if possible; run D10 W when NPO
hypoglycemia	Intraoperative glucose monitoring
hyperglycemia	Intraoperative glucose monitoring and use of insulin infusion if glucose >8 mmol/L
hypotension	Support with fluids; avoid lactate-containing intravenous solutions
sepsis	Standard management
hypothermia	Intraoperative temperature monitoring, warm fluids prior to infusion

Specific Recommendations

- Preop
  - Cardiac workup in Kearns-Sayre or others Liberal fluids and/or IV dextrose
  - Converse with your consultants
- Intraop
  - No significant myopathy
    - Sevoflurane in limited concentrations
  - Significant myopathy
    - May induce with inhaled agent, then switch to TIVA
  - If propofol is used, limit its dose/duration
  - NMB with close monitoring of effect
    - Avoid succinylcholine
  - Regional/local (caution with dosing) and opioids to help reduce requirements
  - Fluids
    - Dextrose containing fluid at maintenance
    - Close glucose monitoring
    - Normal saline, colloid, blood for surgical losses
      - Avoid lactated Ringer's
  - Normothermia
  - PONV prohylaxis
- Postop
  - Monitored care depending on disease and case

Treatment

- No treatments
- Dichloroacetate
  - Trial discontinued due to peripheral toxicity
- CoQ
  - Supports respiratory chain
- L-arginine
  - May have some promising effects
- Symptomatic management

Mitochondrial Disease Special Interest Group and Data Collection

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Dream a Little Dream…

Duke

Pediatric Anesthesia


HELP GET HER OUT OF BED ON SUNDAY AUGUST 30TH
Mitochondrial Disease (MD) is a genetic disorder that robs thousands of Australians of their energy, trapping them in their beds. Help free them by joining Stay In Bed Day on Sunday August 30. Register today at stayinbedday.org.au
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