

<http://www.youtube.com/watch?v=veQAJ4qlltU&feature=related>

- ▶ Pete Strube Candidate for Resolutions Committee Region 3
- ▶ Wilma Gillis Candidate for Region 3 Director
- ▶ Karen Eisenberner Candidate for Vice-President

You Know You Have Reached Middle Age If?

- ▶ While you are appalled by President Clinton's sexual exploits, you admire his stamina
- ▶ You've stopped worrying about the size of your penis and started worrying about the size of your prostate
- ▶ You can use the word osteoporosis in a sentence
- ▶ Your tattoos have folds

New Anesthesia Drugs

Already here or on the Horizon

Major Peter D. Strube
CRNA MSNA APNP AN NP

Comfort Zone

- ▶ Most of us practice our art in the comfort zone
- ▶ New and different ideas tend to pull people from the comfort zone to the scare zone
- ▶ Try new things
- ▶ Enhance your patient outcomes
- ▶ We will be discussing actual drugs---with names not drugs in the XX301-7559PLD stage

Fospropofol (Lusedra)

- ▶ Approved by the FDA on 12/12/08 a pro-drug of propofol
- ▶ Same mechanism of action; except has a slow, smooth and predictable rise in concentration
- ▶ By; Definition: this is a sedative-hypnotic aqueous agent indicated for monitored anesthesia care (MAC) sedation in adult patients undergoing diagnostic or therapeutic procedures.
- ▶ NOT FOR GENERAL
- ▶ This will and has already raised some concern—FDA states that only those trained in delivering anesthesia should use this drug. What about the ago old question?? What about using this in GI clinic

Fospropofol (Lusedra)

- ▶ Standard monitoring
- ▶ IV dosing adults: 6.5mg/kg – followed by supplemental dosing of 1.6mg/kg as needed
- ▶ Initial dose should not exceed 16.5 ml (35mg/cc)
- ▶ $90 \text{ kg} \times 16.5 = 585\text{mg}$
- ▶ Supplemental doses should not exceed 4ml; each additional doses should only be given when needed and no more frequent than every 4 minutes
- ▶ Dose range 60-90 kg
- ▶ Not for Kids
- ▶ Greater than 65 years of age give 75% of dose
- ▶ For every 1.86mg administered one mg of propofol is created
- ▶ What is special: earlier “clear headed”

Fospropofol (Lusedra)

- ▶ Expensive
- ▶ Side effects:
 - ▶ Respiratory Depression 6%; Hypoxemia 5%; Hypotension 5%
- ▶ EXPENSIVE
- ▶ Not comparatively better than propofol and versed
- ▶ Not compatible with versed or Demerol
- ▶ Need to flush line after use
- ▶ Greater than 20% experience paresthesia and cough
- ▶ Paresthesia by their definition included: burning, tingling and stinging
- ▶ This was manifested in the perineal region:: why phosphate preservative

Etomidate --MOC

- ▶ Methoxycarbonyl-etomidate (MOC-etomidate), a new compound derived from the anesthetic etomidate, is as fast-acting and provides the same hemodynamic stability as its parent drug, but does not cause dangerous adrenal gland suppression as etomidate can
- ▶ In the human liver cells, the researchers found that the MOC-etomidate had an in-vitro half-life of 4.4 minutes versus more than 40 minutes for etomidate, and produced carboxylic acid as its only detectable metabolite
- ▶ MOC-etomidate is an etomidate analogue that retains etomidate's important favorable pharmacological properties. However, it is rapidly metabolized, ultra-short acting, and does not produce prolonged adrenocortical suppression following bolus administration

Emend (Aprepitant)

- ▶ A new class of antiemetics is born -- NK-1 receptor antagonists
- ▶ Does not interfere with other antiemetics
- ▶ No dosage adjustments for hepatic or renal compromise
- ▶ Does not effect QT segments
- ▶ Use in caution with CYP3A4 (warfarin) drugs; this is typically related to a three day course in chemo-related treatments
- ▶ Decreases efficacy of hormonal contraceptives
- ▶ Anesthesia is a single dose; 40-80mgs
- ▶ Expensive single 80mg dose is \$125

Emend (Aprepitant)

- ▶ This is an additional adjunct treatment to those refractory to PONV
- ▶ Most side effects are related to prolonged and high doses with little evidence that any effects are related to a single anesthesia dose
- ▶ Top adverse experiences in patients with general anesthesia were;
 - ▶ Anemia, bradycardia, flatulence, hypotension, pruritus, pyrexia
- ▶ Expensive ; Expensive; Expensive; Expensive

Cleviprex

- ▶ New Calcium Channel blocker
- ▶ ?? Dose it's problems outweigh it's benefits
- ▶ Could be a key agent for emergency hypertensive crisis
- ▶ Hypertensive therapy when oral agents not feasible
- ▶ Has a rapid onset and 1-2 minute half-life (15 minutes to total elimination)
- ▶ Could find a spot with cardiac surgery and cardiac patients(?)
- ▶ Maybe Neurosurgery -- Emergency room
- ▶ Vascular selective -- acts specifically on vascular smooth muscle to reduce arterial BP (after load) without inducing myocardial depression

Cleviprex

- ▶ Positives:
- ▶ Non weight based dosing
- ▶ Dose-dependent BP lowering response
- ▶ No dose adjustment for renal or hepatic dysfunction
- ▶ Ready to use vials
- ▶ Can be administered via peripheral line

- ▶ Dosing: 1-2 mg/hr with a double every 90 seconds until goal BP
- ▶ Max dose 16mg/hr

Cleviprex

- ▶ Downside???
- ▶ Lipid based (no more than 1000 mls/24 hours period)
- ▶ \$\$ 4 hours of use then discard
- ▶ Can't be administered with anything else (dedicated line)
- ▶ Contraindicated with soy, egg allergy
- ▶ Contraindicated with hyper lipidemia; lipoid nephrosis, pancreatitis, aortic stenosis
- ▶ Negative inotropic effects—contraindicated in heart failure
- ▶ (but is suppose to not cause any myocardial depression)
- ▶ Not for use with beta blocker withdrawal
- ▶ 2% of patients develop HA/N&V
- ▶ Store refrigerated (not easy access)
- ▶ Photosensitive

Palonosetron (Aloxi)

- ▶ A new 5HT-3 receptor antagonist
- ▶ Remember: this group of drugs compete with serotonin to block binding at the serotonin receptor binding site
- ▶ When the binding site is blocked the ion channel on the receptor closes and calcium influx is stopped, blocking signals to the brain that trigger nausea and vomiting
- ▶ What is special about this 5HT-3???
- ▶ Aloxi binds with both the serotonin site but also a allosteric binding site; this action increases the overall affinity for aloxi by triggering a conformational change. This change also causes a receptor internalization and induces a prolonged inhibition of serotonin binding to the cell surface receptors.

Aloxi

- ▶ What is cool about it?? 40 hour plasma half-life
- ▶ Small single dose --- 0.075 mg single dose
- ▶ Easy to remember dose timing -- before induction of anesthesia in preop over 10 seconds (will cover why shortly)
- ▶ NO information for Peds or OB
- ▶ Warnings::::: do not mix with other drugs
- ▶ Flush line before and after admin ?? PKA – weak acid vs. weak base
- ▶ Risks: 5% QT prolongations; bradycardia 4%; Headache3%
- ▶ Headache (remember imitrex)

Aloxi

- ▶ No real elimination issues
- ▶ Eliminated via renal and some metabolic pathways
- ▶ Dose: each 1.5 ml vial contains 0.075 mg of aloxi and 83 mg of mannitol (and buffers)
- ▶ Contraindications: hypersensitivity
- ▶ Contraindications: ?? Several cardiac disease ???

Voluven

- ▶ A new colloid – used to treat hypovolemia
- ▶ What is the benefit?? What about hespan?
- ▶ Remember hespan has a max dose of 20cc/kg to a max of 1000cc's
- ▶ Voluven has a max dose of 50cc/kg
- ▶ Initial dose should be 10-20cc (not per kg) and observe for signs of a reaction

Voluven

- ▶ Contraindications:
- ▶ Hypersensitivity; fluid overload; CHF; renal failure; dialysis; hypernatremia; hyperchloremia; intracranial bleeding
- ▶ Watch for dilution of blood products
- ▶ Adjust for renal and hepatic patients
- ▶ Number one side effects is pruritus
- ▶ Watch for anaphylactoid and hypersensitive reaction

LIPID Rescue

- ▶ How does this work????
- ▶ Small school of thought is that LA interfere with fatty acid transport into the mitochondria of the cardiac cells which inhibits the heart from performing oxidative phosphorylation and this is what leads to cardiac dysrhythmias
- ▶ Most (and the current) thought pattern is that LIPIDS act as a SINK

The sink – the lipids provide a alternative binding site for the LA

- ▶ Cheap and found by accident – when it is cheap what drug company will fund research

LIPID rescue

- ▶ Cardiac toxicity related to the overdose or intravascular injection of local anesthetics has long been a concern of anesthesia
- ▶ Overdose is characterized by seizures, hypotension, atrioventricular conduction delay, idioventricular rhythms, and eventual cardiovascular collapse
- ▶ Think about who is helping you with the block
- ▶ All local anesthetics potentially shorten the myocardial refractory period, Marcaine has the highest affinity for cardiac tissues (cardiac sodium channels) making marcaine the most likely to participate malignant arrhythmias.
- ▶ Remember B E E R OK B E R

Lipid Rescue

- ▶ First line of defense is to be conservative!!!!
- ▶ If the surgeon asks you what the dose is – go under!!
- ▶ Aspirate prior to injection
- ▶ Check of HEME

- ▶ Data suggests up to 20 out of 10,000 peripheral nerve blocks
- ▶ Data suggests up to 4 out of 10,000 epidural blocks
- ▶ Goal is to prevent complications; with proper injection techniques and careful dosing

- ▶ Remember Madison OB patient a few years ago.....
 The major failure was not identifying the problem

- ▶ Current treatments ACLS, BYPASS, LIPID rescue

Lipid Rescue

- ▶ 2006 lipid rescue was touted as the new Local Anesthetic toxicity rescue treatment
- ▶ Current suggestion includes LIPID available at all facilities
- ▶ Will we ever know more???? Lipids are cheap; drug companies don't want to pay when there will be little if any profit
- ▶ Mechanism of action: several suggested reasons-----
- ▶ Most agree it is a LIPID sink: meaning, lipids reverse local anesthetic cardio toxicity may be increasing cardiac clearance. This nonspecific, observed extraction of local anesthetics from aqueous plasma or cardiac tissue is the lipid sink

Lipid Rescue

- ▶ 20% lipid solution
- ▶ 1.5 ml/kg over 1 minute
- ▶ Follow immediately by an infusion at rate of 0.25mg/kg/min (17.5 ml/min for a 70 kg adult)
- ▶ Repeat dose if no improvement – and double the infusion rate
- ▶ www.lipidrescue.org
- ▶ Airway Management
- ▶ Lipids
- ▶ TX seizures
- ▶ ACLS
- ▶ What about Propofol? Lipid based?

Sugammadex

- ▶ Forms a very tight water soluble complex with steroidal NDMR
- ▶ i.e. ROC > VEC > PANC
- ▶ It is biologically inactive, does not bind to plasma proteins
- ▶ Does not rely on renal excretion
- ▶ WE have always miss-used muscle relaxants (first reported 1979)
- ▶ IV administration results in rapid removal of free drug from the plasma. This action creates a concentration gradient favoring the movement of the NDMR molecules from the NMJ back into the plasma, where they are encapsulated by free sugammadex molecules.

Sugammadex

- ▶ Does not affect SUXX or benzyliisoquinoliniums;
- ▶ If after using sugammadex and paralysis needs to be achieved consider using these drugs
- ▶ SIDE EFFECTS: hypotension; coughing (was from a study when given to awake patients) vomiting, nausea, dry mouth, decreased temperature
- ▶ Expensive
- ▶ Rumor has it;;; it will be packaged with ROC
- ▶ Is traditional Neuromuscular function monitoring needed?

Sugammadex

- ▶ Dose examples: ROC 1.2mg/kg administered and three minutes later 16mg/kg of sugammadex given, this provides faster onset/offset profile than suxx
- ▶ Remember FRC
- ▶ Will this change the face of anesthesia??

Xenon

- ▶ A age old treatment has always been on the side lines
- ▶ Inert gas
- ▶ 1939 first experiments were for the US Navy
- ▶ Rediscovered in 1990

- ▶ Xenon has the ability to interact with cell proteins and cell membranes; this action is presumably responsible for its anesthetic potency
- ▶ Xenon also inhibits plasma membrane calcium pump, which may be responsible for an increase in neuronal calcium and altered excitability

- ▶ Xenon seems to inhibit nociceptive responsiveness of the spinal dorsal horn neurons and effect that may be mediated by inhibition of NMDA receptors

- ▶ Basically we are not 100% sure how it works

XENON

- ▶ MAC 0.71
- ▶ Fast on fast off
- ▶ No apparent effect on the gut (mesenteric vascular resistance)
- ▶ Minimal effects on cardiovascular tissues
- ▶ Very rare NOBLE gas
- ▶ Recovered from the atmosphere through a process called air liquification
- ▶ This rarity leads to expense \$10/Liter (100 x more than N2O)
- ▶ Triple the cost of SEVO and ISO
- ▶ To be useful needs to be administered via a rebreathing circuit via the lowest possible gas flows

XENON

- ▶ The cost differences could be adjusted and would become progressively smaller the longer the duration of anesthesia. The rate of xenon consumption declines overtime as the body tissues become saturated in a closed rebreathing system
- ▶ Nitrogen must be washed out first (5-minutes)
- ▶ Hypnotic effects achieved in 1.5/min reaching desired effects in 8 min
- ▶ Less diffusion hypoxia
- ▶ Does not prolong NDMB
- ▶ Non-flammable and non explosive

XENON

- ▶ Go Green:
- ▶ The lifetime of N₂O in the atmosphere is 120 years and has actually been proven to contribute to global warming
- ▶ Xenon is being part of the atmosphere and manufactured from liquefied air, doesn't add to pollution – it is simply back to where it started
- ▶ If all yearly production (6 million liters) were used only for anesthesia only 400,000 anesthetics could be performed
- ▶ We need to create a effective way to recycle this

Tham

- ▶ Are the days of treating trauma acidosis with bicarb over?
- ▶ Tham supplements the buffering capacity of the blood bicarbonate system, accepting a proton, generating bicarbonate and decreasing the partial pressure of carbon dioxide in arterial blood
- ▶ It rapidly distributes through the extra cellular space and slowly penetrates the intracellular space, except for erythrocytes and hepatocytes and it is excreted by the kidney
- ▶ Key; THAM works continuously and maintains its buffering power in the presence of Hypothermia

Tham

- ▶ Tham rapidly restores pH and acid base regulation in acidaemia caused by carbon dioxide retention or metabolic acid accumulation, which have the potential to impair organ function
- ▶ In large dose it may cause respiratory depression and hypoglycemia
- ▶ Dosage: Loading dose of THAM acetate 0.3 mol/l in the treatment of acidaemia
- ▶ Example: ml of 0.3mol/L soln = KG x base deficit
- ▶ Max dose is 15 mmol/kg or 3.5L of a 0.3mol/l soln in a 70 kg patient
- ▶ $70\text{kg} \times -9.1 = 637\text{cc}$

THAM

- ▶ In early treatment THAM can save lives by maintain normal pH
- ▶ This treatment keeps the homeostatic mechanisms of acid-base regulation to assume normal function
- ▶ THAM has been used in the periphery for years and small doses
- ▶ The war in IRAQ and Afghanistan have pushed it's use to be the major treatment in trauma

Indocyanine Green

- ▶ Old drug; so not really new; but a new use that we should be aware of
- ▶ For those of that are old we remember this drug in cardiac outputs before the thermo dilution.
- ▶ Used in Neurosurgery
- ▶ Ophthalmologic clinics for retinal imaging

- ▶ In Neurosurgery it allows the surgeon to record flow images

- ▶ Dose: 6.25mg (single ampoule is 12.5mg in 5cc) so half a amp

- ▶ Iodine based so you may get a reaction with patients allergic to shellfish and iodine.

- ▶ Mild pulse dosimeter interference
- ▶ Wait for surgeons signal
- ▶ Administer rapid IV bolus with flush

Blood Substitutes

- ▶ Not really? Should really be called oxygen transport substitutes
- ▶ Examples: Hemopure, Oxygent, Polyheme and Perftoran
- ▶ They are either perfluorocarbon or hemoglobin based
- ▶ Most products vary in the level of clinical phase trials
- ▶ US military experimenting with blood substitutes as well as dried blood
- ▶ Israel military in conjunction with core dynamics has a done all the initial research on freeze-dried blood; your own blood stored for you

Corneal Abrasions During General Anesthesia

- ▶ The cornea is the clear, dome-shaped outer area of the eye. It lies in front of the colored part of the eye (iris) and the black hole in the iris (pupil). The outermost layer of the eyeball consists of the cornea and the white part of the eye (sclera). A corneal abrasion is basically a superficial cut or scrape on the cornea. A corneal abrasion is not as serious as a corneal ulcer, which is generally deeper and more severe than an abrasion
- ▶ To diagnose a corneal abrasion, a topical **anesthetic** with a yellow **dye** called fluorescein is placed into the eye. Under blue **cobalt** light, the part of the cornea abraded will be stained by the dye and is easily seen by the examiner. The area and depth of the abrasion can be easily seen under a special microscope called a **slit lamp biomicroscope**. If a microscope is not available, then a blue light called a Burton lamp may be used
- ▶ Topical nonsteroidal anti-inflammatory drugs (NSAIDs) such as diclofenac (Voltaren) and ketorolac (Acular) are modestly useful in reducing pain from corneal abrasions
- ▶ If antibiotics are used, ointment (e.g., bacitracin [AK-Tracin], erythromycin, gentamycin [Garamycin]) is more lubricating than drops and is considered first-line treatment. In patients who wear contact lenses, an antipseudomonal antibiotic (e.g., ciprofloxacin [Ciloxan], gentamycin, ofloxacin [Ocuflox]) should be used, and contact lens use should be discontinued. Clinical trial data are lacking, but it is recommended that contact lenses be avoided until the abrasion is healed and the antibiotic course completed.

Questions

► Thank you

