

# New Anesthesia Drugs

Already here or on the Horizon

Tranquilizers 100	Induction Agents 105	Anxiolytic Agents 110	Obstetrics 115
Tranq. Reversal 120	Major Tranquilizers 125	Antiemetics 130	Hematological 135
Muscle Relaxants 140	Narc. / Tranq. Combo. 145	Antibiotics 150	Diuretics 155
Potent Antagonists 160	Vasopressors 165	Antibiotics 170	Radiology 175
Narcotics 180	Hypotensive Agents 185	Steroids 190	Misc. 195
Neuroleptic Antagonism 200	Local Anesthetics 205	Electrolytes 210	Invasive Line Taps 215

LTC Peter D. Strube

CRNA MSNA APNP ARNP DNAP(c)

Assistant Professor Rosalind Franklin University

Things are in evolution and only getting faster and faster!



RECOVERY ROOM

DEDICATED BY  
NORWEGIAN  
CRUISE LINES

# Dedicated to:

*Thomas G Healey, RN, CRNA, MA*  
St Mary's University  
Died January 5, 2014

**Navy Corpsman Vietnam**



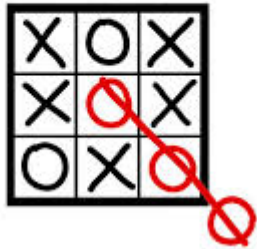
# Financial Disclosure

There is no financial conflicts with this presentation.

Lecturing about a topic does not constitute endorsement of any product. Please take the time to research each topic for more information.

Mentioning a product or company does NOT represent endorsement.

**THINK  
OUTSIDE  
THE BOX**



# Think outside the BOX

We can no longer sit by the wayside, we must make ourselves better.

Keep a OPEN Mind!

Multimodal

Synergy

Preemptive

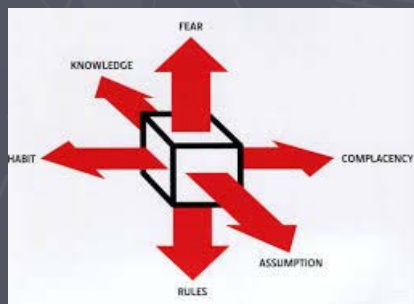
Standard, Policy, Guideline, Suggestion???

Zofran



FDA Alerts!

FDA and Codeine?



U.S. Department of Health & Human Services

**FDA U.S. Food and Drug Administration**

What's New on the FDA Drugs Site

February 5, 2015

- [FDA's GDUFA Public Hearing on Policy Development](#)
- [Drug Firm Annual Registration Status](#) (updated)
- [Drug Firm Annual Registration Status Download File](#) (updated)
- [FDA Drug Shortages](#)

- [Atropine Sulfate Injection](#) (Updated - Currently in Shortage)
- [Bupivacaine Hydrochloride \(Marcaine, Sensorcaine\) Injection](#) (Updated - Currently in Shortage)
- [Cefazolin Injection](#) (Updated - Currently in Shortage)
- [Dextrose 5% Injection Bags](#) (Updated - Currently in Shortage)
- [Dextrose Injection USP, 70%](#) (Updated - Currently in Shortage)
- [Ethinorgestrel Injection](#) (Updated - Currently in Shortage)

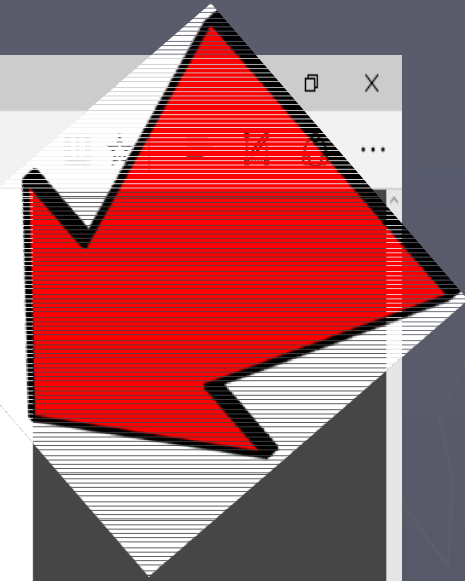
these pediatric patients was comparable to the prevention of vomiting in patients 4 years of age and older.

**Postoperative Nausea and Vomiting: Prevention of Postoperative Nausea and Vomiting:**

**Adult Studies:** Adult surgical patients who received ondansetron immediately before the induction of general balanced anesthesia (barbiturate: thiopental, methohexital, or thiamylal; opioid: alfentanil or fentanyl; nitrous oxide; neuromuscular blockade: succinylcholine/curare and/or vecuronium or atracurium; and supplemental isoflurane) were evaluated in two double-blind US studies involving 554 patients. ZOFTRAN Injection (4 mg) I.V. given over 2 to 5 minutes was significantly more effective than placebo. The results of these studies are summarized in Table 8.

**Table 8. Prevention of Postoperative Nausea and Vomiting in Adult Patients**

	Ondansetron 4 mg I.V.	Placebo	P Value
Study 1			
Emetic episodes:			
Number of patients	136	139	
Treatment response over 24-h postoperative period			
0 Emetic episodes	103 (76%)	64 (46%)	<0.001
1 Emetic episode	13 (10%)	17 (12%)	
More than 1 emetic episode/rescued	20 (15%)	58 (42%)	
Nausea assessments:			
Number of patients	134	136	
No nausea over 24-h postoperative period	56 (42%)	39 (29%)	
Study 2			
Emetic episodes:			





**Tablets**

**Sprinkles**

**Topamax®  
(topiramate)**

Abstract

Send to

Eur J Neurol. 2004 Jul;11(7):475-7.

High-dose riboflavin treatment is efficacious in migraine prophylaxis: an open study in a tertiary care centre.

Boehnke C, Reuter U, Flach U, Schuh-Hofer S, Einhäupl KM, Arnold G.

Author information

Abstract

The aim of this study was to investigate the efficacy of riboflavin for the prevention of migraine. An open label study was performed in a specialized outpatient clinic. Patients received 400 mg riboflavin capsules per day. Headache frequency, duration, intensity and the use of abortive drugs were recorded at baseline and 3 and 6 months after treatment. Headache frequency was significantly reduced from 4 days/month at baseline to 2 days/month after 3 and 6 months (P < 0.05). The use of abortive drugs decreased from 7 units/month to 4.5 units/month after 3 and 6 months of treatment (P < 0.05). In contrast, headache hours and headache intensity did not change significantly. We could demonstrate a significant reduction of headache frequency following riboflavin treatment. In addition, the number of abortive anti-migraine tablets was reduced. In line with previous studies our findings show that riboflavin is a safe and well-tolerated alternative in migraine prophylaxis.

PMID: 15257686 [PubMed - indexed for MEDLINE]



Publication Types, MeSH Terms, Substances

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- Botulinum toxin type A as migraine preventive treatment in patients previously [Headache. 2008]
- Prophylaxis of migraine, transformed migraine, and cluster headache with topir [Headache. 2002]
- Riboflavin prophylaxis in pediatric and adolescent migraine. [J Headache Pain. 2009]
- Review Supplementation with Riboflavin (Vitamin B2) for Migr; [Int J Vitam Nutr Res. 2015]
- Review [Prophylactic treatments of migraine]. [Rev Neurol (Paris). 2000]



# 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

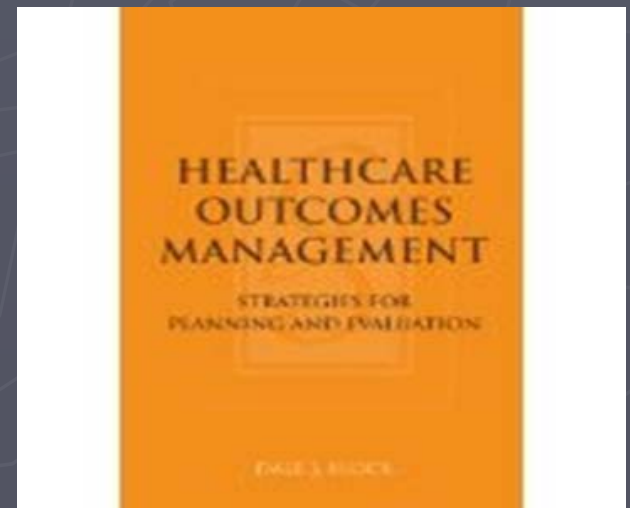
# AFE – September 29, 2014 (presentation) Dr. B Leighton, Cooper, Otto (abstract fall 2013)

41 G8P3-39 weeks at 31 min ACLS: Given A-OK at 1mg/8mg/30mg  
Survived and left hospital with small neuro deficits

28 G2P1-39 weeks at ?? Min ACLS: Given A-OK at 0.8mg/4mg/30mg  
Survived with no neuro issues

Thromboxane/serotonin

Use this in conjunction to current treatments.  
At this time this is a adjunct to get the patient  
to return to circulation.



# AANA Journal June 2015

## Role of Esmolol in Perioperative Analgesia and Anesthesia: A Literature Review

*Megan Harless, CRNA, MSN*

*Caleb Depp, CRNA, MSN*

*Shawn Collins, CRNA, DNP, PhD*

*Ian Hewer, CRNA, MSN, MA*

*Use of opioids to provide adequate perioperative analgesia often leads to respiratory depression, nausea, vomiting, urinary retention, pruritus, and opioid-induced hyperalgesia, with the potential to increase length of stay in the hospital. In an effort to reduce perioperative opioid administration yet provide appropriate pain relief, researchers began to study the use of esmolol beyond its well-known cardiovascular effects. Perioperative esmolol has been shown to*

*reduce anesthetic requirements, decrease perioperative opioid use, decrease the incidence of postoperative nausea and vomiting, lead to an earlier discharge, and increase patient satisfaction. This article provides a review of the literature on the use of esmolol as an adjunct for perioperative analgesia and anesthesia.*

*Keywords: Esmolol, opioid sparing, perioperative analgesia and anesthesia.*

Can you do a anesthetic without narcotics?

# Not Everything is it appears? Labor Epidurals going away?

Blair et al **Patient-controlled analgesia for labor using remifentanyl: a feasibility study?**

Remifentanyl PCA with a bolus dose in the range 0.25–0.5  $\mu\text{g kg}$  and a lockout time of 2 min appears a safe and effective drug for use in labor in patient-controlled analgesia systems



# Is Nitrous Back? 2009

The position of the American College of Nurse-Midwives that women should have access to a variety of measures to assist them in coping with the challenges of labor. Among these should be nitrous oxide, which is commonly used in many other countries.



Lowe, NK. The nature of labor pain. *Am J Obstet Gynecology* 2002;186(5):S16–24.

Marmor TR, Krol DM. Labor pain management in the United States: Understanding patterns and the issue of choice. *Am J Obstet Gynecology* 2002;186:S173-80.

Rooks JP. Nitrous oxide for pain in labor – why not in the United States? *Birth* 2007;34:3-.

Rosen MA. Nitrous oxide for relief of labor pain: A systematic review. *Am J Obstet Gynecology* 2002;186:S110-26

Declercq ER, Sakala C, Corry MP, Applebaum S. Listening to Mothers II: Report of the Second National U.S. Survey of Women's Childbearing Experiences. New York: Childbirth Connection, October 2006, p. 31.

# Crazy?



## Ancient drug yielding new use

'Magic mushrooms' being tested by UW as option for cancer patients, others

DAVID WAHLBERG  
dwahlberg@madison.com, 608-252-6125

Amid the institutional labs, offices and classrooms of Rennebohm Hall, home to UW-Madison's School of Pharmacy, lies a room with an oversized sofa, nature scenes on the walls, a chime and a drum on an inlay

Exp.:

Lot:

04-B184-7/R5 (3377)



NDC 55292-102-01

100 Tablets

**Desoxyn<sup>®</sup>**  
(methamphetamine hydrochloride tablets, USP)

**5 mg** Ⓜ Ⓡ only

DISPENSE THE ENCLOSED MEDICATION GUIDE WITH EACH PRESCRIPTION.  
GO TO [www.recordatirarediseases.com](http://www.recordatirarediseases.com)

Each tablet contains 5 mg methamphetamine hydrochloride.

See package insert for full prescribing information.

Store below 86°F (30°C).

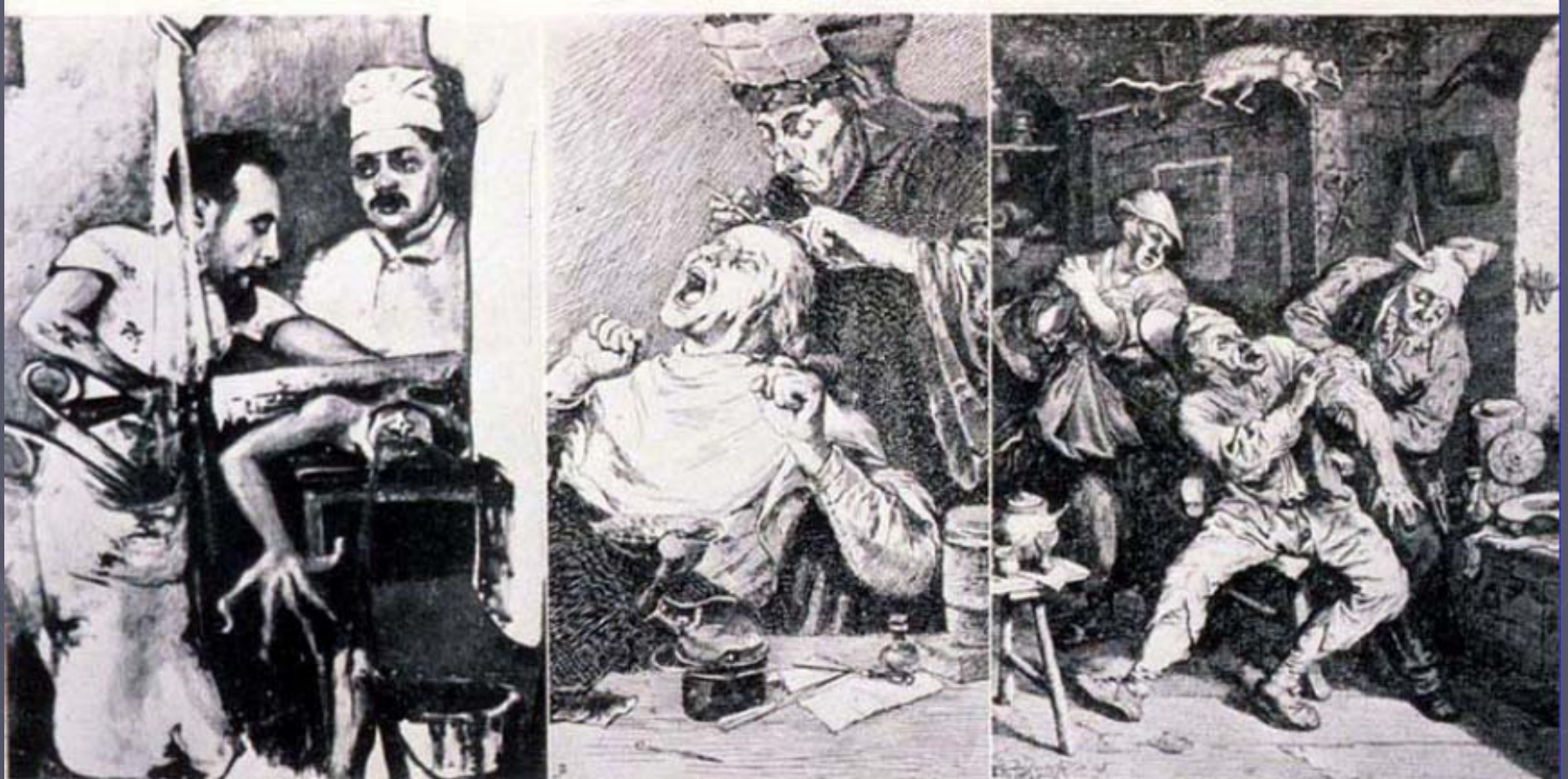
Dispense in a USP tight, light-resistant container.

Do not accept if seal over bottle opening is broken or missing.

Manufactured by: AbbVie LTD

For: Recordati Rare Diseases Inc.  
Lebanon, NJ 08833, U.S.A.

# Surgery Before Anesthesia and Pharmacology



Mural of Dr. Villander, Hôtel de Dieu, Paris.

A

From *Behind the Doctor*, by Logan Clendenning, published by Alfred A. Knopf.

B

From *Devils, Drugs and Doctors*, by Howard W. Haggard, M.D., published by Harper and Brothers.

C

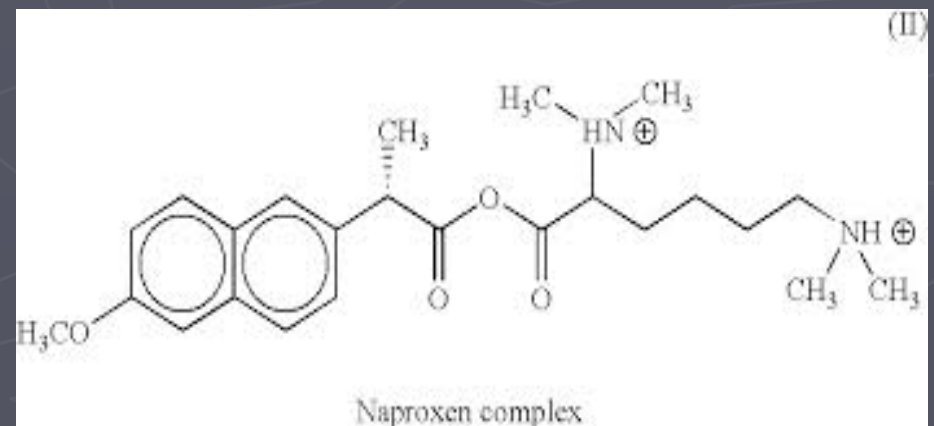
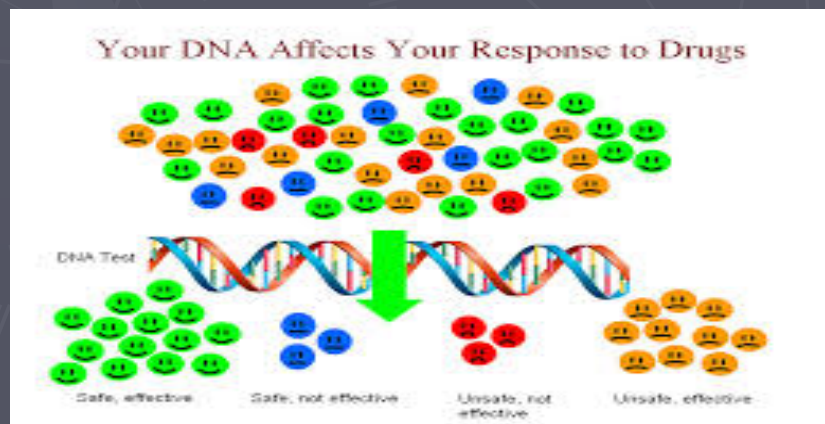
PICTORIAL RECORDS OF THE AGONY ENDURED IN OPERATIONS BEFORE THE ADVENT OF ANESTHESIA

- A. A surgeon cutting with his big saw.
- B. A very painful operation of the seventeenth century.
- C. A surgeon torturing his patient.

# Think outside the BOX— Think Differently!

Old Drugs, New Ways  
New Drugs, Old Battles!

## Pharmacogenetics----Micron Technology



## Dogma?

Dogma is a principle or set of principles laid down by an authority as incontrovertibly true. It serves as part of the primary basis of an ideology or belief system, and it cannot be changed or discarded



Traumatic injury is a common problem, with over five million worldwide deaths from trauma per year. An estimated 10 to 20% of these deaths are potentially preventable with better control of bleeding. Damage control resuscitation involves early delivery of plasma and platelets as a primary resuscitation approach to minimize trauma-induced coagulopathy. Plasma, red blood cell and platelet ratios of 1:1:1 appear to be the best substitution for fresh whole blood; however, the current literature consists only of survivor bias-prone observational studies.

# MASSIVE TRANSFUSION

Early Recognition of Massive Transfusion (MT) Patients

Most patients requiring emergency unmatched blood in ED will need MT

Predictors (3/4 70% 4/4=85% of MT)

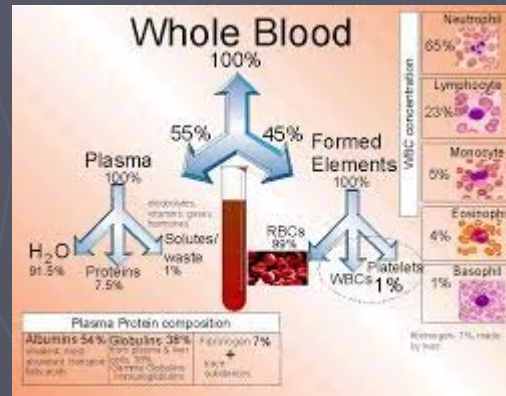
SBP < 110 mmHg

HR > 105

HCT < 32

pH < 7.25

1:1:1



## Combat Anesthesia: A Case Report of a Gunshot Wound and New Trauma Protocols

MAJ Peter D. Strubo, CRNA, MSNA, APNP, ARNP, ANG, USA  
MAJ Andrew D. Perkins, CRNA, MSNA, ANG, USA

Revolutionary innovations and technical advances in the disciplines of medicine, surgery, and anesthesia are inextricably connected to military conflict. The demonstrated lifesaving value of these novel approaches in high-acuity trauma has provided the impetus for translation of these elements into injury care in the civilian environment. One element of this battlefield medical revolution is the implementation and refinement of forward surgical care. All US military services have unique configurations of this surgical team to match their expeditionary capacity. The US Army Forward Surgical Team (FST) is a small, mobile surgical unit fielded since the 1950s, but not ubiquitously used until the current

contingency operations in southwest Asia. The FST has been used in a variety of ways during the current conflict with or without augmentation by a forward support medical company, Area Support Medical Company, Forward Support Medical Company also known as C-Med, and Brigade Support Medical Company. Forward support medical companies have often been employed to provide a surgical capability for patients in austere operational environments and to optimize casualty survival in situations of high-risk operations and/or with potential for protracted evacuation.

**Keywords:** Forward surgical care, nurse anesthesia, trauma.

In the US Army Forward Surgical Team (FST) model, the surgical team performs lifesaving interventions, specifically surgical hemorrhage control for battlefield casualties within the "golden hour" of injury. After initial resuscitation, casualties are then "packaged" for medical evacuation to a higher level of care. The FST by doctrine includes 20 staff members, including 3 registered nurses, 3 licensed practical nurses, 2 surgical technicians, 4 medics, 1 detachment sergeant, 1 administrative officer, 4 surgeons (3 general and 1 orthopedic), and 2 Certified Registered Nurse Anesthetists (CRNAs). By doctrine of the Field Manual 4-02-25 (March 2003) and Army Training and Evaluation Program 8-518-10, the team is capable of continuous operations with a divisional or nondivisional medical company for up to 72 hours, with a planned caseload of 30 critical patients.<sup>1</sup> A functional operating room (OR) can be established within 1 hour of being on the scene and broken down to move to a new location within 2 hours of ceasing operations. The FST can sustain surgery for 24 total operating-hours and has the ability to separate into 2 component teams that function independently at disparate locations. In these split operations, the team must be split to maintain functionality by maintaining logistic, operational, surgical, and anesthesia support with CRNA coverage.<sup>1</sup> Nurses first provided anesthesia to wounded soldiers during the Civil War. Nurse anesthetists have been the main providers of anesthesia care to US military personnel on the front lines in the history of modern warfare. In 1914, Dr George Crile, a pioneer in American surgery, and his nurse-anesthetist, Agatha Hodgins, who became

the founder of the American Association of Nurse Anesthetists (AANA), went to France with the American Ambulance Group to assist in the establishment of hospitals that would provide care for the sick and wounded of the Allied Forces. Nurse Ellen Orkin was a prime example of the courage, dedication, and leadership exhibited by nurse anesthetists in support of our troops during World War II. In a field that was in its infancy, she received rudimentary training and became a nurse anesthetist in 3 days. She then landed with the 164th General Hospital supporting the main body of the invasion of Normandy on D-Day armed only with vials of sodium pentothal. She continued to serve troops with honor during World War II, as did her sister. The commitment and sacrifice of the CRNA community in combat surgical support have been maintained through the current operations of Iraqi Freedom and Enduring Freedom. In 2003, LTC Steve Hendrix, CRNA, participated in the rescue mission of PFC Jessica Lynch, COL Gale Pollock, CRNA, was promoted to major general and became the 22nd chief of the US Army Nurse Corps, the third CRNA to serve in that position. Later, she was appointed acting surgeon general of the US Army.<sup>2,3</sup>

Trauma resuscitation protocols have changed drastically in the past decade secondary to the analyses of lessons learned in the conflicts in both Iraq and Afghanistan, and subsequent changes in clinical practice have occurred. In the fourth US revision of Emergency War Medicine published in 2013, US Army Surgeon and General Trauma Consultant Col Brian Eastridge noted:

## Far Forward Anesthesia and Massive Blood Transfusion: Two Cases Revealing the Challenge of Damage Control Resuscitation in an Austere Environment

David Gaskin, CRNA, MHS  
Nicholas A. Kroll, CRNA  
Alyson A. Ochs, RN  
Martin A. Schreiber, MD  
Prakash K. Pandalai, MD

Since the beginning of Operation Enduring Freedom and Operation Iraqi Freedom, the US military has treated more than 51,000 casualties and sustained more than 6,600 deaths. The past decade of conflict has solidified major advances in the use of blood component therapy and the liberal use of fresh whole blood during damage control resuscitation. This resuscitation strategy, combined with far forward damage control surgery, rapid aeromedical evacuation, and major improvements in critical care air transportation and personal protective equipment has led to a 90% to 92% survival rate in US casualties. We describe 2 cases treated by a Forward Surgical Team serving in Afghanistan during Operation Enduring Freedom

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A massive blood transfusion (MT) is defined as transfusion of greater than 10 U of packed red blood cells (PRBCs) in the first 24 hours following injury. The Joint Theater System is the military institution responsible for reporting and ensuring optimal care of the injured warfighter. This system reports that 9% of all casualties admitted to a combat support hospital—the highest level of medical care in the combat theater—receive an MT.<sup>2</sup> Findings of a large prospective observational trial suggest

in 2014. Both patients suffered severe trauma and required massive blood transfusion and damage control surgery. In describing these 2 cases, we wish to share our experience with damage control resuscitation in an austere environment, as well as advocate for the critical role of the Certified Registered Nurse Anesthetist in advancing the knowledge and execution of this lifesaving strategy in both military and civilian trauma centers. In addition, we suggest alternatives to the current transfusion strategy, which will mitigate limitations currently encountered.

**Keywords:** Damage control resuscitation, Forward Surgical Team, fresh whole blood.

that civilian trauma patients experience an MT rate of 1%, representing a large number of individuals at risk for casualties.<sup>4</sup> Civilian statistics demonstrate that of those trauma patients who die, 46% die of central nervous system (CNS) injuries, 21% die of hemorrhage, 16% die of a combination of CNS injury and hemorrhage, 9% die of multiple organ failure, and 3% of other causes.<sup>5</sup> Despite the fact that hemorrhage is a less common cause of death than CNS injury, it is the most common cause of preventable death in both civilian and military casualties.<sup>5,6</sup>

We describe 2 cases treated by a Forward Surgical Team (FST) serving in Afghanistan during Operation Enduring Freedom in 2014. Both patients suffered severe trauma and required MT and damage control surgery. One patient died despite exhaustive measures, and patient was transferred to the combat support hospital following stabilization. In describing these 2 cases, we wish to (1) share our experience with damage control resuscitation in an austere environment, (2) advocate for the critical role of the Certified Registered Nurse Anesthetist (CRNA) in advancing the knowledge and execution of this lifesaving strategy in both military and civilian trauma centers, and (3) suggest alternatives to

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AANA Journal • August 2015 • Vol. 83, No. 4 247

# Fluid Resuscitation for Hemorrhagic Shock in Tactical Combat Casualty Care

## TCCC Guidelines Change 14-01

28 June 2014

### Conclusions

1. The preferred fluids for resuscitation of casualties in hemorrhagic shock, in descending order of preference, are:

- Whole blood
- 1:1:1 plasma, RBCs, and platelets
- 1:1 plasma and RBCs
- Reconstituted dried plasma, liquid plasma, or thawed plasma alone  
or RBCs alone
- Hextend
- Lactated Ringers or Plasma-Lyte A

# Tranexamic Acid

New to Ortho World

A competitive inhibitor of plasminogen, and in high concentrations a non-competitive inhibitor of plasmin

Less transfusions -- reported 50%

Trauma: Antifibrinolytic agent

Increased trauma survival in prospective analysis

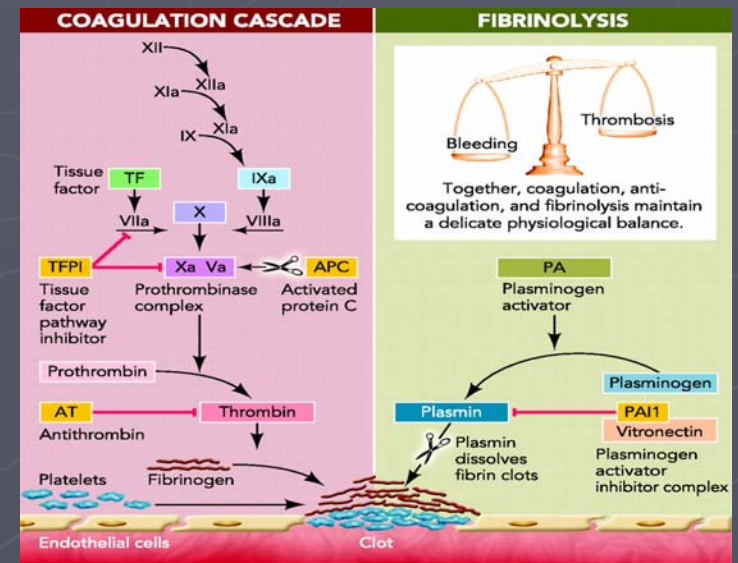
Can't have blood products, Hextend in same line

Give within 3 hours- 1gm in 100mL NS over 10 mins

Then start infusion of 1gm in 100mL NS over 8 hours

Pump rate 12.5ml/hr

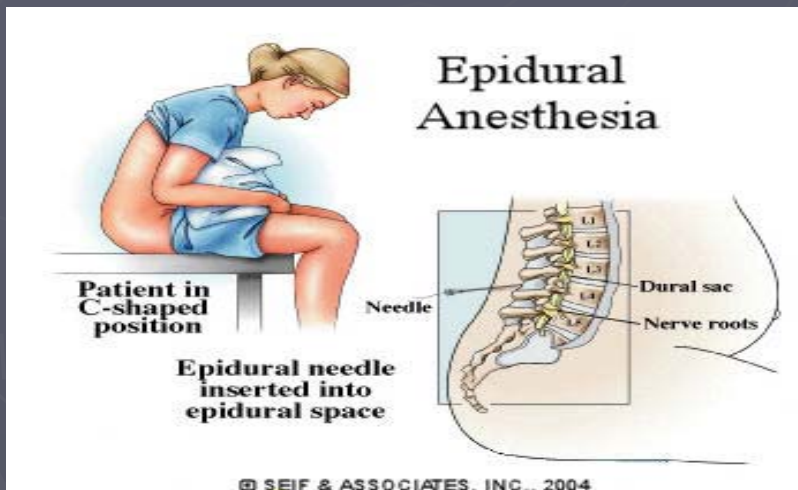
Further doses can be given, though not supported by literature



Anesth Analg. 2005 Nov;101(5):1516-20.

Prophylactic intravenous ondansetron and dolasetron in intrathecal morphine-induced pruritus: a randomized, double-blinded, placebo-controlled study.

Anesthesiology, 2015; 15(18)



**30 minutes before injecting narcotic spinal or epidural**

# New MH Drug? Ryanodex

The drug, an injectable suspension of dantrolene sodium, will be available in 250 mg single-use vials containing the active ingredient in a lyophilized powder.

According to Eagle Pharmaceuticals, Ryanodex can be prepared and administered in less than one minute, compared with 15 to 20 minutes for conventional dantrolene.



The cost for a patient receiving Ryandex treatment for a MH crisis (based off 2.5mg/kg in a 70kg patient) is \$1,610 verses \$700 with generic dantrolene. This cost does not include additional doses of dantrolene that will be required

This research and orphan drug status is leading to additional research... for example for heat stroke:



# Side Effects: MDMA--Ecstasy

Succinylcholine (X is a trigger) should be used cautiously given the risk of compounding the malignant hyperthermia like effects of the drug, raising intracranial pressure or potentially worsening hyperkalemia

The Harborside Hotel | Bar | (47 unread) - pstrube3000 - 3,4-Methylenedioxyet x +

ncbi.nlm.nih.gov/pubmed/22089516

[Eur J Anaesthesiol](#), 2012 Jan;29(1):42-9. doi: 10.1097/EJA.0b013e32834d9427.

**3,4-Methylenedioxymethamphetamine (Ecstasy) increases the sensitivity of the contractile apparatus to calcium ions in both malignant hyperthermia-susceptible and normal skeletal muscle fibres.**

Gerbershaagen MU<sup>1</sup>, Missler G, Schütte JK, Starosse A, Graf BM, Wappler F, Zink W.

Author information

**Abstract**

**CONTEXT AND OBJECTIVES:** The present study was designed to investigate whether 3,4-methylenedioxymethamphetamine (MDMA, 'Ecstasy') increases the sensitivity of the contractile apparatus to calcium in muscle fibres from malignant hyperthermia-susceptible and malignant hyperthermia-negative pigs, whether it causes calcium ion release from the sarcoplasmic reticulum and whether it inhibits calcium reuptake into the sarcoplasmic reticulum.

**DESIGN:** Experimental study, using a model of porcine saponin-skinned fibres.

**RESULTS:** Administration of MDMA in concentrations of 1, 2 and 4 mmol l<sup>-1</sup> did not result in relevant force transients in skinned muscle fibres of malignant hyperthermia-susceptible or malignant hyperthermia-negative pigs. Furthermore, MDMA in these concentrations did not alter calcium ion loading of the sarcoplasmic reticulum in either group. With regard to changes in the calcium ion sensitivity of the contractile proteins, however, MDMA dose-dependently increased (pCa<sub>50</sub>) values (negative decadic logarithm of [Ca<sup>2+</sup>] at which isometric force is half-maximal) in both groups.

**CONCLUSION:** In the present study, we were able to demonstrate that MDMA dose-dependently increases the sensitivity of the contractile apparatus to calcium in both malignant hyperthermia-susceptible and malignant hyperthermia-negative fibres. Consequently, the malignant hyperthermia status should not affect the calcium sensitivity of the contractile apparatus. However, the increased calcium sensitivity is an important finding that must be appreciated, particularly in relation to the agonistic effect of MDMA at the nicotinic acetylcholine receptor, which increases intracellular calcium ion concentrations.

PMID: 22089516 DOI: 10.1097/EJA.0b013e32834d9427  
[PubMed - indexed for MEDLINE]

Publication Types, MeSH Terms, Substances

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### Dantrolene Use in 3,4-Methylenedioxymethamphetamine ("Ecstasy")-Mediated Hyperthermia

*To the Editor:*—We read with great interest the study by Fiege *et al*<sup>1</sup> published in the November 2003 issue of ANESTHESIOLOGY. Although we applaud the authors' attempt to shed some light on the controversial use of dantrolene in 3,4-methylenedioxymethamphetamine (MDMA)-mediated hyperthermia, several flaws in the design and interpretation of their results cast doubts on their conclusions.

Our strongest criticism of this study is in the authors' use of a combination therapy (dantrolene, sodium bicarbonate, and hyperventilation) to determine the role of dantrolene in MDMA-mediated hyperthermia. The positive results attributed to dantrolene in figure 2 of this study, a reduction in partial pressure of carbon dioxide and an increase in pH, can be explained by the use of sodium bicarbonate and hyperventilation alone without any contribution from dantrolene. More notably, we believe that the failure to show a reduction in core body temperature (their fig. 2C) with their treatment supports the idea that dantrolene has no role in MDMA-mediated hyperthermia. Because malignant hyperthermia-normal swine were similarly affected (although slightly less so), we are curious why the authors did not study their treatment regimen in these animals. Because malignant hyperthermia-normal animals were not genetically susceptible, dantrolene would not have been expected to be beneficial and could have differentiated the effects of dantrolene from the other treatments given.

Also, questions arise with the authors' sole reliance on clinical criteria in their definition of malignant hyperthermia. Based on their criteria for malignant hyperthermia, any agent that uncouples oxidative phosphorylation, irrespective of its effects on calcium dihydropyridine and ryanodine receptors (RyR), would meet the criteria for mediating malignant hyperthermia. Although we agree that the study by Fiege *et al*<sup>1</sup> suggests an exaggerated hyperthermic response to MDMA in malignant hyperthermia-susceptible swine, the significant alterations in the partial pressure of carbon dioxide, pH, and temperature seen in the malignant hyperthermia-normal swine suggests that the effect is largely not mediated through RyR complexes.

Finally, in the design of their study, Fiege *et al*<sup>1</sup> chose to use sequential dosing of 0.5 mg/kg MDMA every 20 min until a cumulative dose of 12 mg/kg was achieved. MDMA-induced hyperthermia is well

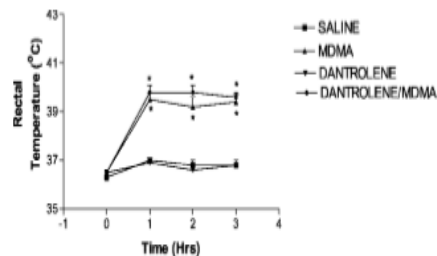


Fig. 1. Effects of dantrolene (2.5 mg/kg, intraperitoneal) 30 min before 3,4-methylenedioxymethamphetamine (MDMA; 40 mg/kg, subcutaneous) on rat rectal temperatures. Data are presented as mean  $\pm$  SEM (n = 6). \* Significantly different from saline and dantrolene-only groups (P < 0.001).

(fig. 1). The inability of dantrolene to block MDMA-induced hyperthermia suggests that this is not a true "malignant" hyperthermia and that other mechanisms are evoked after MDMA exposure.

Controlled trials have not been performed to determine whether the few purported clinical successes using dantrolene to control MDMA-induced hyperthermia are due to dantrolene alone *versus* all other supportive, first-line cooling therapies. The inability of dantrolene to block the thermogenic effects of MDMA in both our study and that of Fiege *et al*<sup>1</sup> suggests that RyR-mediated calcium cycling is not the mediator of the thermogenic effects of MDMA. The authors' recommendation to use dantrolene in all cases of MDMA-induced hyperthermia is not supported by their data or other current scientific literature and may result in overreliance on a drug that may not benefit critically ill patients with MDMA-induced hyperthermia.

Daniel E. Rusyniak, M.D., Matthew L. Banks, Pharm.D., Edward M. Mills, Ph.D., Jon E. Sprague, Ph.D.\* Ohio Northern University, Ada, Ohio. j-sprague@onu.edu

# 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”

Clinical Therapeutics/Volume 38, Number 1, 2016

## Magnesium Sulfate Plus Lidocaine Reduces Propofol Injection Pain: A Double-blind, Randomized Study

Jiehao Sun, MD; Riyong Zhou, MD; Wendong Lin, MD; Jiahao Zhou, MD; and Weijian Wang, MD

Department of Anesthesiology, 1st Affiliated Hospital, Wenzhou Medical University, Wenzhou, China

### ABSTRACT

**Purpose:** Propofol injection can cause distressing pain, and no method can inhibit it completely. Neither lidocaine nor magnesium sulfate ( $MgSO_4$ ) was sufficient to prevent pain from the injection of propofol. This prospective, double-blind, placebo-controlled study was designed to investigate the efficacy of the  $MgSO_4$  plus lidocaine on suppressing propofol injection pain.

**Methods:** Three hundred women received 300 mg  $MgSO_4$  (Group M), 40 mg lidocaine (Group L), or 300 mg  $MgSO_4$  plus 40 mg lidocaine (Group M+L). This was followed by administration of 50 mg propofol. Pain scores, behavior-related responses, and diameter of the vein were recorded following the injection of propofol.

**Findings:** Patients in Group M + L had lower pain scores. Patients' behavior-related responses in Group M + L were also better compared with the other groups. There were no differences in pain scores between Group L and Group M. The target vein diameter change in Group M and Group M + L was more obvious than in Group L.

priority for improvement.<sup>1</sup> Minimizing propofol injection pain is an important clinical goal because it may influence a patient's perception of quality and acceptability of anesthesia. Several measures have been used to reduce the occurrence of propofol injection pain, including the addition of lidocaine with tourniquet; cooling or warming the propofol; diluting the propofol solution; injection of propofol into a large vein; or prior injections of meperidine, metoclopramide, magnesium, thiopental, ketamine, methylene blue, or a  $\beta$ -blocker.<sup>1-7</sup> We have not found a method that suppresses injection pain completely.

Tourniquet causes dilation of veins, and, interestingly, vein size is an important factor in propofol injection pain.<sup>8</sup> A meta-analysis<sup>1</sup> suggested that use of a rubber tourniquet and lidocaine application before propofol injection was most effective to prevent injection pain. Dae et al<sup>9</sup> demonstrated that higher doses of lidocaine can achieve more analgesia, but the incidence of pain can be still as high as 36.8% when a tourniquet combined with 100 mg lidocaine is applied.<sup>1,8</sup>

Most studies have concluded that the intensity of

# Remimazolam

- ▶ Analogue of Midazolam

- ▶ that utilizes the ester design.
- ▶ Broken down by nonspecific ester hydrolysis

- ▶ Designed for out patient procedures as well as EGD/C-Scope area

- ▶ Linear Clearance superior to Versed

- ▶ Better sedation with less side effects of Versed

- respiratory and cardiac events

- ▶ **6mg loading Dose followed by 3 mg maintenance doses**

- ▶ Crazy but initial studies have not change in ventilation or oxygenation with remidmazolam with NO supplemental oxygen applied.....

## Competitive Product Profile for Remimazolam

General anaesthesia

Product Profiles	Remimazolam	Propofol	Sevoflurane
Rapid time to peak effect	✓	✓	✓
Rapid offset	✓	✓	✓
Predictable recovery time	✓	✓	✓
Early discharge	✓	✓	✓
Low respiratory depression	✓	✗	✗
Cardiostability	✓	✗	✗
Early recovery to full cognition	✓	✗	✗
Reversal agent available	✓	✗	✗
Low re-sedation risk after reversal	✓	-	-
No (low) pain on injection	✓	✗	-
Low risk of excitation†	✓	✓	✗
No risk of theatre contamination	✓	✓	✗
No risk of atmospheric pollution	✓	✓	✗
Simple equipment to handle	✓	✓	✗

†Strong indicator of record

# Paion Presents Positive Remimazolam Phase III Colonoscopy Results at the 2016 American College of Gastroenterology Annual Scientific Meeting

« 3 Pharmaceutical Stocks t...

How mHealth Will Change t... »

Chelsea Pratt • October 19, 2016

[Add Comment](#)



PAION AG, a specialty pharma company (ISIN DE000A0B65S3; Frankfurt Stock Exchange Prime Standard: PA8) today announces that data on the clinical results of remimazolam's U.S. Phase III colonoscopy trial were presented in the Colon/Stomach oral session at the 2016 American College of Gastroenterology (ACG) Annual Scientific Meeting in Las Vegas. Remimazolam is an innovative, ultra-short-acting benzodiazepine anesthetic/sedative for which positive topline data from this trial were published in June 2016.

Douglas Rex, M.D., Indiana University, Indianapolis, IN, U.S., principal investigator of this Phase III trial, presented the results.

The Phase III trial enrolled a total of 461 patients at 13 U.S. sites

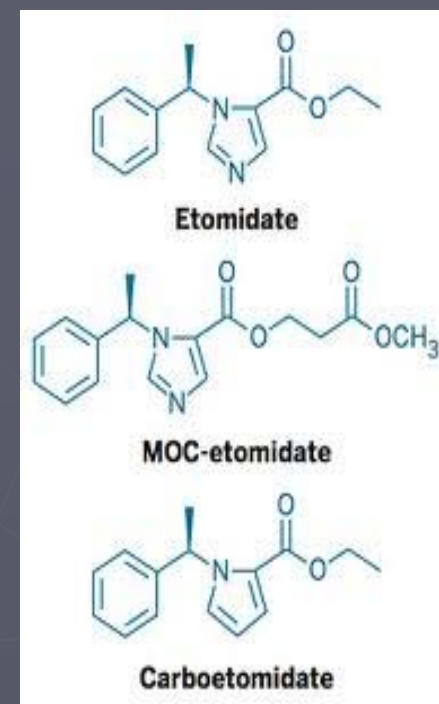
^ Rogers WK, McDowell TS (December 2010). "Remimazolam, a short-acting GABA(A) receptor agonist for intravenous sedation and/or anesthesia in day-case surgical and non-surgical procedures". *IDrugs : the Investigational Drugs Journal*. **13** (12): 929–37. PMID 21154153.

# 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



[Curr Pharm. Des.](#)  
2012;18(38):6253-6.

**Novel etomidate derivatives.**  
[Sneyd JR](#)<sup>1</sup>.

# Carboetomidate

- ▶ Analogue of etomidate
- ▶ When compared to MOC it has slow onset and difficult to formulate.
- ▶ ??? Benefit ???

# Phaxan



Water-based clear, colorless solution that is easy to manufacture.

Like propofol, the current standard for intravenous anesthesia, Phaxan™ is a fast onset and offset intravenous anesthetic but, unlike propofol, there is no accumulation with repeat dosing.

Phaxan™ is twice as potent as propofol but it causes less blood pressure fall than propofol with a six times higher safety margin.

A clinical trial involving dose finding and comparison with propofol was commenced in December 2013.

Interesting thought... old stuff coming back??



# Dexamethasone



- ▶ Steroids are useful as adjuvant therapy for pain
- ▶ Steroids can directly reduce pain in concert with opioid use and allow for a reduction in dose
- ▶ Steroids reduce pain by inhibiting prostaglandin synthesis
- ▶ Steroids have been shown to reduce spontaneous discharge in an injured nerve, which reduces neuropathic pain.
- ▶ **What if we could add it to our Blocks? Increase our Duration!**

## Anesthesiology. 2011;115:575-88

De Oliveira GS Jr, Almeida MD, Benzon HT, McCarthy RJ

- ▶ Perioperative single dose systemic dexamethasone for postoperative pain: a meta-analysis of randomized controlled trials
- ▶ Doses of 0.1 mg/kg or less are great for PONV but don't help with pain relief.
- ▶ Doses of about 0.15 mg/kg cover PONV *and* reduce postoperative pain and opioid demand.
- ▶ Doses above 0.2 mg/kg don't get you any more pain relief. An exception may be greater pain relief with movement (e.g. early ambulation in total joint patients?).
- ▶ Giving dexamethasone *preoperatively* improves pain relief considerably more than giving it after induction. (Optimally 1-2 hours before incision.)
- ▶ In general, we need not worry about side effects with 0.15 mg/kg any more than we do with current PONV doses.

British Journal of Anaesthesia 107 (3): 446–53 (2011)  
Advance Access publication 14 June 2011 · doi:10.1093/bja/aer159



# Effect of dexamethasone on the duration of interscalene nerve blocks with ropivacaine or bupivacaine

K. C. Cummings III<sup>1,2\*</sup>, D. E. Napierkowski<sup>4</sup>, I. Parra-Sanchez<sup>2</sup>, A. Kurz<sup>2</sup>, J. E. Dalton<sup>2,3</sup>, J. J. Brems<sup>5</sup> and D. I. Sessler<sup>2</sup>

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## Editor's key points

- This trial demonstrates a difference in block

**Background.** Pain after shoulder surgery is often treated with interscalene nerve blocks. Single-injection blocks are effective, but time-limited. Adjuncts such as dexamethasone may help. We thus tested the hypothesis that adding dexamethasone significantly prolongs the duration of ropivacaine and bupivacaine analgesia and that the magnitude

Downloaded from [http://bj.a.oup.com/](#)

## Dexamethasone with bupivacaine increases duration of analgesia in ultrasound-guided interscalene brachial plexus blockade

Peter A. Vieira, Istvan Pulai, George C. Tsao, Poornachandran Manikantan, Brunella Keller and Neil Roy Connelly

**Background and objective** Dexamethasone has been shown to prolong the duration of postoperative analgesia when given as an adjunct for peripheral nerve blocks. However, it has not been evaluated when given in conjunction with bupivacaine and clonidine to provide blockade of the brachial plexus at the interscalene level. The purpose of this investigation was to determine whether the addition of dexamethasone to interscalene brachial plexus block would prolong the duration of sensory analgesia in a group of patients undergoing outpatient shoulder arthroscopy.

**Methods** This prospective, randomized, double-blind investigation was performed on 88 individuals undergoing shoulder arthroscopy. Patients received interscalene brachial plexus block using 20 ml of bupivacaine 5 mg ml<sup>-1</sup> with 1:200 000 epinephrine and clonidine 75 µg. Patients were randomly assigned to receive either dexamethasone 8 mg or 0.9% NaCl as an adjuvant to the mixture. After discharge, patients recorded pain scores and analgesic consumption in a diary and estimated the time at which they perceived that the sensory block from the interscalene brachial plexus block resolved. This was based on pain, recovery of sensation and strength in the arm. Variables measured included demographics,

timed pain intensity measurements, postoperative analgesic consumption, duration of analgesia and patient satisfaction.

**Results** Dexamethasone prolonged median sensory (1457 vs. 833 min,  $P < 0.0001$ ) and motor (1374 vs. 827 min,  $P < 0.0001$ ) blockade compared with the control. At 24 h, the dexamethasone group had lower median verbal analogue scale scores compared with control (3.0 vs. 6.0). At 48 h, the two groups had similar median pain scores (4.0 vs. 5.0, dexamethasone vs. control, respectively). The opioid requirement in oxycodone equivalency was lower in the dexamethasone group than in the control group for the first 24 h, and similar thereafter. Median patient satisfaction scores were not significantly different between the two groups at 48 h (9.5 vs. 8.0, dexamethasone vs. control, respectively).

**Conclusion** The addition of dexamethasone to a bupivacaine-epinephrine-clonidine interscalene block prolongs sensory block and reduces opioid use.

*Eur J Anaesthesiol* 2010;27:285–288

**Keywords:** ambulatory, anaesthesia, analgesia, brachial plexus, clonidine, orthopaedic, regional

Received 7 June 2009 Revised 2 November 2009

Accepted 5 November 2009

### Introduction

Regional anaesthesia has gained much popularity in outpatient orthopaedic surgery. Increasing duration of local

addition of epinephrine prolongs duration of subcutaneous infiltration of local anaesthesia.<sup>2</sup>

# Emend (Aprepitant) PDNV



- ▶ A new class of antiemetic's is born -- NK-1 receptor antagonists
- ▶ Does not interfere with other antiemetic's
- ▶ 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
- ▶ Two additional NK-1 Drugs: Casopitant, Rolapitant

# Rolapitant

VARUBI is a substance P/neurokinin 1 (NK1) receptor antagonist indicated in combination with other antiemetic agents in adults for the prevention of delayed nausea and vomiting.

The recommended dosage is 180 mg Rolapitant administered approximately 1 to 2 hours prior to the start of chemotherapy

Administer in combination with dexamethasone and a 5-HT<sub>3</sub> receptor antagonist,

TESARO in-licensed it: Dec. 2010;  
2009 FTC **OPKO** ordered it  
divested from  
"the bust-up": **SP** Schering-Plough...  
now branded as... **VARUBI**

FDA Approved  
09.02.2015

**Rolapitant H Cl**  
 $C_{25}H_{29}ClF_6N_2O_3$

...now, a competitor to...

**EMEND**<sup>®</sup>  
(aprepitant)

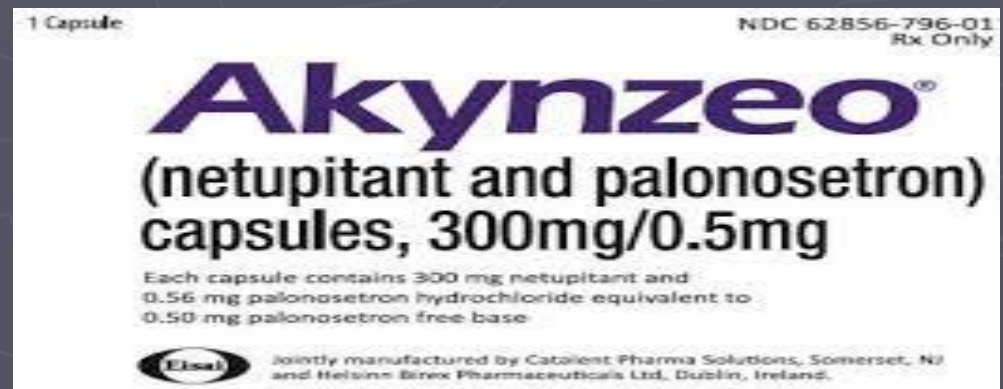
MERCK

The graphic features a purple unicorn standing on a molecular structure, a Schering-Plough logo, and images of EMEND product packaging (a box and a vial).

# Akynzeo

Akynzeo, a combination product of netupitant and palonosetron

Each capsule contains 300 mg of netupitant, and palonosetron hydrochloride equivalent.



# Marinol



MARINOL should not be used if you are

- ▶ allergic to dronabinol or any of its ingredients,
  - including marijuana and sesame oil
- ▶ Most patients respond to 5 mg three or four times daily.
- ▶ Marinol has been shown to provide increased pain relief when taken in combination with opioid pain relievers, according to [ClinicalTrials.gov](https://clinicaltrials.gov). The active ingredient in Marinol, THC, is believed to bind with pain receptors to reduce the transmission of pain through the spinal cord and brain

# Olanzapine as an antiemetic: is an atypical antipsychotic that belongs to the thienobenzodiazepine class.

Olanzapine cost:

- Rapidly disintegrating tab 5mg: ~ \$1.00
- Rapidly disintegrating tab 10mg: ~ \$1.15
- Tab 5mg: \$0.10
- Tab 10mg: \$0.20
- IM injection: \$25.25

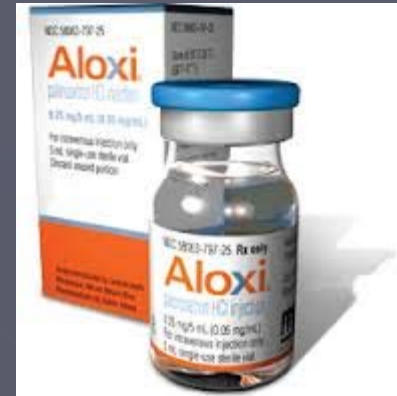


We only have a very small amount of information about the use of olanzapine IV,  
and none of it in the periop period.....

Most Studies looked at it as compared to Zofran.....



# Palonosetron (Aloxi) PDNV



- ▶ 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)

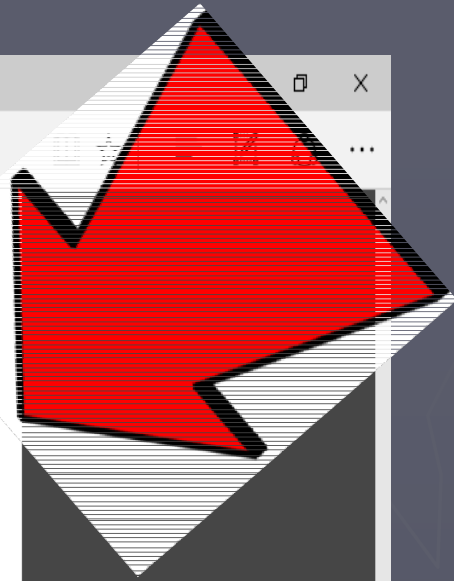
these pediatric patients was comparable to the prevention of vomiting in patients 4 years of age and older.

**Postoperative Nausea and Vomiting: *Prevention of Postoperative Nausea and Vomiting:***

**Adult Studies:** Adult surgical patients who received ondansetron immediately before the induction of general balanced anesthesia (barbiturate: thiopental, methohexital, or thiamylal; opioid: alfentanil or fentanyl; nitrous oxide; neuromuscular blockade: succinylcholine/curare and/or vecuronium or atracurium; and supplemental isoflurane) were evaluated in two double-blind US studies involving 554 patients. ZOFTRAN Injection (4 mg) I.V. given over 2 to 5 minutes was significantly more effective than placebo. The results of these studies are summarized in Table 8.

**Table 8. Prevention of Postoperative Nausea and Vomiting in Adult Patients**

	Ondansetron 4 mg I.V.	Placebo	P Value
Study 1			
Emetic episodes:			
Number of patients	136	139	
Treatment response over 24-h postoperative period			
0 Emetic episodes	103 (76%)	64 (46%)	<0.001
1 Emetic episode	13 (10%)	17 (12%)	
More than 1 emetic episode/rescued	20 (15%)	58 (42%)	
Nausea assessments:			
Number of patients	134	136	
No nausea over 24-h postoperative period	56 (42%)	39 (29%)	
Study 2			
Emetic episodes:			



# Versed



Anesthesia and Analgesia 2016; 122:656

Meta-Analysis of studies from 1974-2014

Drastically reduced PONV, especially with preop and small dose 30 minutes before extubation.



## Clinical Research Article

Korean J Anesthesiol 2012 April 62(4):343-349  
<http://dx.doi.org/10.4097/kjae.2012.62.4.343>

# The antiemetic effect of midazolam or/and ondansetron added to intravenous patient controlled analgesia in patients of pelviscopic surgery

Dae Seong Kim, Gill Hoi Koo, Hyun Kang, Chong Wha Baek, Yong Hun Jung, Young Cheol Woo, Jin Yun Kim, and Sun Gyoo Park

Department of Anesthesiology and Pain Medicine, College of Medicine, Chung-Ang University, Seoul, Korea

**Background:** We made a comparative study on the antiemetic effect of midazolam and ondansetron added to intravenous patient-controlled analgesia (PCA) using fentanyl with gynecologic patients undergoing pelviscopic surgery.

**Methods:** The PCA using 20 µg/kg of fentanyl was started in all groups postoperatively. A dose of 16 mg of ondansetron was added to the PCA of group O (n = 30). A dose of 5 mg of midazolam was added to the PCA of group M (n = 30). While 16 mg of ondansetron and 5 mg of midazolam were added to the PCA of group MO (n = 30). Total volume of the PCA was 60 ml, and the PCA system was programmed to deliver 0.5 ml/h of continuous doses and a 0.5 ml bolus on demand, with a 15 minutes lockout interval. The incidence of postoperative nausea and vomiting (PONV), sedation score, visual analog scale (VAS) for pain, and rescue drug dose for PONV were investigated at the postanesthesia care unit (PACU), 6 hours, and 24 hours after recovery.

**Results:** The incidence of PONV in group MO was significantly lower than in group O at PACU, 24 hours after recovery ( $P < 0.05$ ). The sedation score and VAS pain score showed no differences among all groups.

# The last 30 minutes Versed

Lee Y, Wang JJ, Yang YL, Chen A, Lai HY.  
Midazolam vs ondansetron for preventing  
postoperative nausea and vomiting: a  
randomized controlled trial. *Anaesthesia*.  
2007;62(1):18-22.

# Non-Pharmacologic Methods for PONV



- ▶ Acupuncture—really exciting information!
- ▶ Acupressure
  - over "P6" point of wrist (3cm prox. to distal wrist crease, between the tendons of palmaris longus and flexor carpi radialis)
  - over K-K9 acupuncture point (middle phalanx of 4<sup>th</sup> finger) applied bilaterally
- ▶ Alcohol Pad—Quease Ease!



**September 2013; Anesthesia and Analgesia: Aromatherapy as Treatment for Postoperative Nausea: A Randomized Trial Hunt, Ronald MD<sup>\*</sup>; Dienemann, Jacqueline PhD, RN<sup>†</sup>; Norton, H. James PhD<sup>‡</sup>; Hartley, Wendy MSN, RN<sup>§</sup>; Hudgens, Amanda BSN, RN<sup>||</sup>; Stern, Thomas MD<sup>1</sup>; Divine, George PhD<sup>#</sup>**

# Oxygen

- ▶ Hypoxia triggers cortical afferents which triggers the vomiting center which leads to the act of vomiting
- ▶ One specific study showed a decreased rate of PONV
- ▶ A second study trying to prove the first could not either prove or disprove the first study
- ▶ Increased O<sub>2</sub> levels (less than 80%) in orthopedics have been shown to decrease infection rates in total joints
- ▶ Interesting thoughts?



# Oxygen



Hypoxia triggers cortical afferents which triggers the vomiting center which leads to the act of vomiting

Enhanced Rec... brydges prese... Enhanced Rec... Fluid Managem... FluidMgmt.pdf Eras | Enhancer... Enhanced Rec... ppt Perioperati... Effect of in

ncbi.nlm.nih.gov/pubmed/23719611

U.S. National Library of Medicine  
National Institutes of Health

Advanced

Format: Abstract

Anesthesiology, 2013 Aug;119(2):303-16. doi: 10.1097/ALN.0b013e31829aaff4.

**Effect of intraoperative high inspired oxygen fraction on surgical site infection, postoperative nausea and vomiting, and pulmonary function: systematic review and meta-analysis of randomized controlled trials.**

Hovaquimian F<sup>1</sup>, Lysakowski C, Elia N, Tramèr MB.

Author information

**Abstract**

**BACKGROUND:** Intraoperative high inspired oxygen fraction (FIO<sub>2</sub>) is thought to reduce the incidence of surgical site infection (SSI) and postoperative nausea and vomiting, and to promote postoperative atelectasis.

**METHODS:** The authors searched for randomized trials (till September 2012) comparing intraoperative high with normal FIO<sub>2</sub> in adults undergoing surgery with general anesthesia and reporting on SSI, nausea or vomiting, or pulmonary outcomes.

**RESULTS:** The authors included 22 trials (7,001 patients) published in 26 reports. High FIO<sub>2</sub> ranged from 80 to 100% (median, 80%); normal FIO<sub>2</sub> ranged from 30 to 40% (median, 30%). In nine trials (5,103 patients, most received prophylactic antibiotics), the incidence of SSI decreased from 14.1% with normal FIO<sub>2</sub> to 11.4% with high FIO<sub>2</sub>; risk ratio, 0.77 (95% CI, 0.59-1.00). After colorectal surgery, the incidence of SSI decreased from 19.3 to 15.2%; risk ratio, 0.78 (95% CI, 0.60-1.02). In 11 trials (2,293 patients), the incidence of nausea decreased from 24.8% with normal FIO<sub>2</sub> to 19.5% with high FIO<sub>2</sub>; risk ratio, 0.79 (95% CI, 0.66-0.93). In patients receiving inhalational anesthetics without prophylactic antiemetics, high FIO<sub>2</sub> provided a significant protective effect against both nausea and vomiting. Nine trials (3,698 patients) reported on pulmonary outcomes. The risk of atelectasis was not increased with high FIO<sub>2</sub>.

**CONCLUSIONS:** Intraoperative high FIO<sub>2</sub> further decreases the risk of SSI in surgical patients receiving prophylactic antibiotics, has a weak beneficial effect on nausea, and does not increase the risk of postoperative atelectasis.

**Comment in**

Benefits and risks of intraoperative high inspired oxygen therapy: firm conclusions are still far off. [Anesthesiology. 2014]  
Does high oxygen concentration reduce postoperative infection? [Anesthesiology. 2014]  
In reply. [Anesthesiology. 2014]  
Intraoperative high inspired oxygen fraction: are there real benefits? [Anesthesiology. 2014]

PMID: 23719611 DOI: 10.1097/ALN.0b013e31829aaff4  
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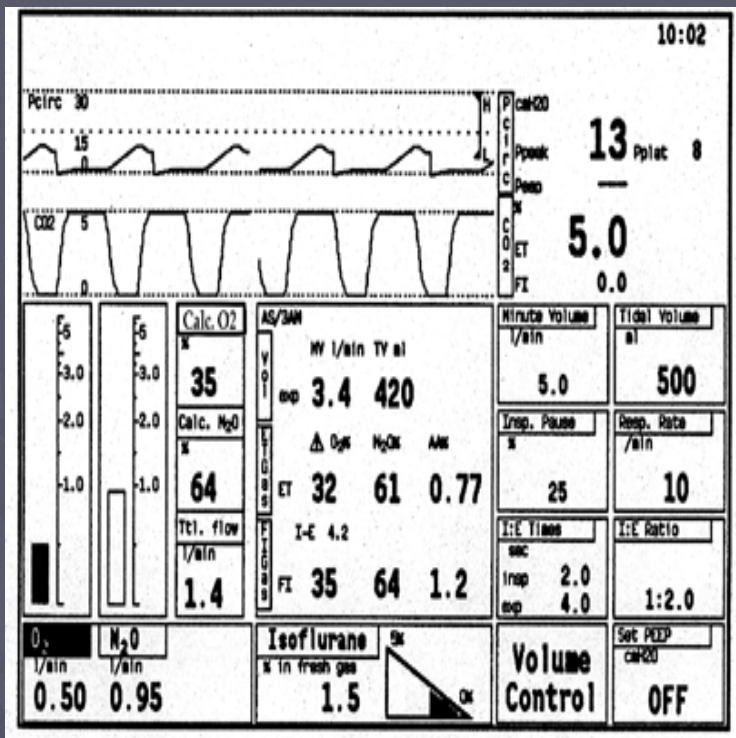
Intraoperative high inspired oxygen fraction: are there real benefits? [Anesthesiology. 2014]  
Surgical site infection and the routine use of perioperative hyperoxia in a genera [JAMA. 2004]  
Benefits and risks of intraoperative high inspired oxygen therapy: firm conc [Anesthesiol. 2014]  
Review [Supplemental oxygen for the prevention of postoperat [Rev Esp Anesthesiol Reanim. 2008]  
Review Effect of intra-operative high inspired oxygen fraction on surgical : [J Hosp Infect. 2016]

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Review Integrated approach to colorectal anastomotic leakage [World J Gastroenterol. 2016]  
Cardiac surgery, a right target for hyperoxia? [Crit Care. 2016]  
Electrical Impedance Tomography-guided PEEP

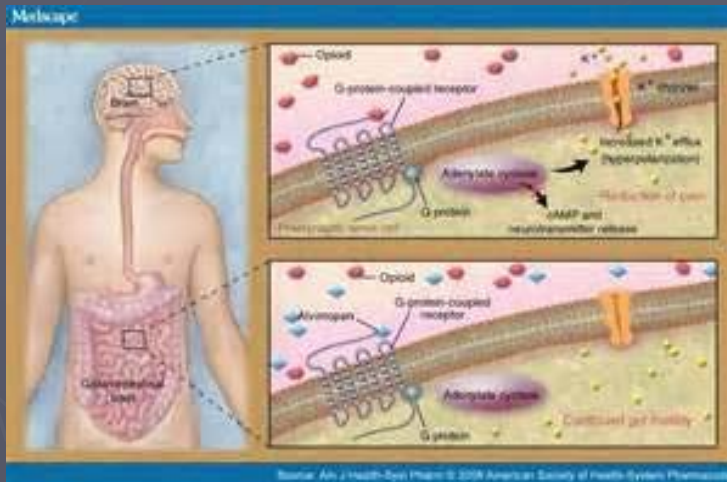
12:21 PM 9/16/2016

# Perioperative clinical factors & immune function



- ▶ Supplemental perioperative oxygen improves postop outcomes
- ▶ FiO<sub>2</sub> of 0.8 doubles subcut O<sub>2</sub> tension & halves postop wound infection rate
- ▶ **Supplemental O<sub>2</sub> ↓ PONV after laparoscopies & laparotomies**

# Pre-operative Alvimopan (Entereg)



## Alvimopan

- $\mu$ -Opioid antagonist that is restricted from crossing the blood-brain barrier
- Blocks peripheral gastrointestinal side effects (eg, ileus, constipation) without compromising CNS activity
- Oral dosing
  - Low systemic absorption
  - High  $\mu$ -receptor affinity
  - Appropriate for patients with chronic pain

CNS, central nervous system.  
Schmidt WK. Am J Surg. 2001;182(5A suppl):275-285.

## Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration: Application to Healthy Patients Undergoing Elective Procedures

*An Updated Report by the American Society of Anesthesiologists Committee on Standards and Practice Parameters*

**P**RACTICE Guidelines are systematically developed recommendations that assist the practitioner and patient in making decisions about health care. These recommendations may be adopted, modified, or rejected according to clinical needs and constraints and are not intended to replace local institutional policies. In addition, Practice Guidelines developed by the American Society of Anesthesiologists (ASA) are not intended as standards or absolute require-

ments, and their use cannot guarantee any specific outcome. Practice Guidelines are subject to revision as warranted by the evolution of medical knowledge, technology, and practice. They provide basic recommendations that are supported by a synthesis and analysis of the current literature, expert and practitioner opinion, open forum commentary, and clinical feasibility data.

This update includes data published since the Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration were adopted by the ASA in 1998 and published in 1999.\*

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Updated by the American Society of Anesthesiologists (ASA) Committee on Standards and Practice Parameters, Jeffrey L. Apfelbaum, M.D. (Chair), Chicago, Illinois; Robert A. Caplan, M.D., Seattle, Washington; Richard T. Connis, Ph.D., Woodinville, Washington; Burton S.

# Practice Guidelines for Preoperative Fasting and the Use of Pharmacologic Agents to Reduce the Risk of Pulmonary Aspiration (Am Soc of Anesthesiologists, 2010)

Minimum preoperative fasting for healthy people

Clear liquids – two hours

Water, fruit juice without pulp, clear tea, black coffee

Light meal (toast + liquid) – six hours

Regular meal (fried or fatty food) – eight hours

# Pre-operative PO fluid





Ann R Coll Surg Engl, 2011 Oct; 93(7): 504-507.  
doi: 10.1308/147870811X13137608455136

PMCID: PMC3604918

# The role of carbohydrate drinks in preoperative nutrition for elective colorectal surgery

C Jones,<sup>1</sup> SA Badger,<sup>2</sup> and R Hannon<sup>1</sup>

[Author information](#) [Article notes](#) [Copyright and License information](#)

See letter "[The role of carbohydrate drinks in preoperative nutrition: comment 2](#)" in volume 95 on page 82.  
See letter "[The role of carbohydrate drinks in preoperative nutrition: comment 1](#)" in volume 95 on page 82.  
This article has been [cited by](#) other articles in PMC.

## Abstract

Go to:

### INTRODUCTION

Traditionally, patients have been fasted from midnight on the night before elective surgery. With the advent of the enhanced recovery programme for elective colorectal surgery, there has been a major change in established practice with patients able to continue with clear fluids up to two hours prior to surgery and solids up to six hours prior to surgery. It has been suggested that nutritional supplements in the immediate pre-operative period enhance post-operative recovery. The aim of this review was therefore critically to appraise the evidence available regarding the use of pre-operative carbohydrate (CHO) supplements for elective colorectal surgery.

"colorectal surgery", singly or in combination. To ensure an up-to-date literature search, the search was restricted to the last ten years. To maximise the search, backward chaining of reference lists from retrieved papers was also undertaken. Only English language articles were included.

### CONCLUSIONS

The use of CHO drinks pre-operatively in colorectal surgery is both safe and effective. There is no increased risk of aspiration and it results in a shorter hospital stay, a quicker return of bowel function and less loss of muscle mass. On the basis of this evidence, the use of pre-operative CHO drinks should be standard in elective colorectal patients. Further research is nevertheless required for those with diabetes mellitus.

**Keywords:** Colorectal surgery, Preoperative carbohydrate nutrition

Traditionally, patients have fasted from midnight before elective surgery. This ensures an empty stomach, thereby helping protective laryngeal reflexes and reducing complications such as aspiration pneumonia. Enhanced recovery for elective colorectal surgery permits clear fluids and solids two and six hours respectively prior to surgery. Nutritional supplements pre-operatively are safe and alter the immune and catabolic response to surgery, enhancing post-operative recovery.<sup>1-3</sup>

Fasting depletes glycogen stores, increasing the demand for amino acids. The endocrine response of insulin resistance to fasting is central to the catabolic surgical response, resulting in reduced insulin stimulated glucose uptake in skeletal muscle and adipose tissue, increased glucose release and hyperglycaemia. Hyperglycaemia is associated with more post-operative complications. Pre-operative carbohydrate (CHO) drinks may reduce insulin resistance by maintaining and improving whole-body protein balance and muscle function.

This review aimed critically to appraise the evidence available regarding the use of pre-operative CHO supplements for elective colorectal surgery.

### Methods

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- Pre-operative oral carbohydrate loading in colorectal surgery: a randomized controlled trial. [Colorectal Dis. 2006]
- The use of mechanical bowel preparation in elective colorectal surgery. [Ulster Med J. 2007]

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- The role of carbohydrate drinks in preoperative nutrition for elective colorecta... PubMed
- The effect of 1 mg folic acid supplementation on clinical outcomes in female mig... PubMed
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- folic acid migraine (26) PubMed
- Effects of inhaled nitric oxide and oxygen in high-altitude pulmonary edema. PubMed

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Ann R Coll Surg Engl (vertical text on left margin)

# Blood Pressure

The BEST treatment of choice for beta-blocker overdose is?

- A. Glucagon
- B. Methylene Blue
- C. Esmolol
- D. Vasopressin



# Glucagon

- ▶ Glucagon is produced in the alpha cells of the pancreas.
- ▶ Glucagon enhances the formation of cAMP.
- ▶ Glucagon is used to increase myocardial contractility and heart rate in the setting of beta-blocker toxicity.
- ▶ Glucagon enhances automaticity in the nodal conduction system without increasing automaticity in the ventricles (unlike sympathomimetic).
- ▶ Glucagon stimulates catecholamine release and has been used as a diagnostic tool in pheochromocytoma.
- ▶ Dose:
  - ▶ 1-5 mg IV slowly
  - ▶ Infusion: 25–75 mcg/min

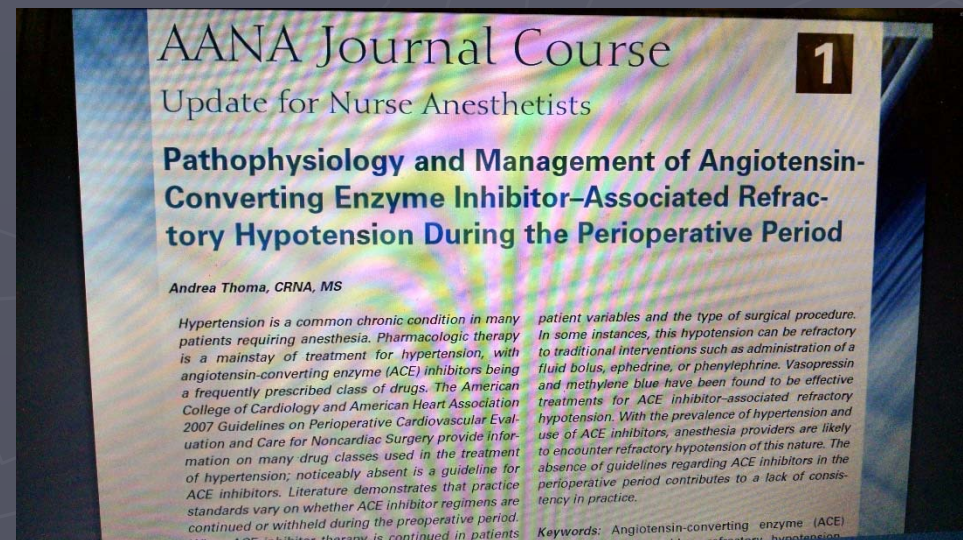


**Glucagon must be reconstituted immediately prior to administration.**

Dosing source: [A Practical Approach to Cardiac Anesthesia](#) by Frederick A. Hensley, Glenn P. Gravlee, Donald E. Martin

# Hypotensive Thought Pattern

- ▶ What is your order for treating Hypotension????
- ▶ 0 fluids
- ▶ 1 and 2; Neo and ephedrine
- ▶ 3 methylene blue
- ▶ 4 epi chip shots (5-10mcg)—Guy Weinberg Paper!
- ▶ 5 vasopressin
- ▶ What is 6 for you?
- ▶ ?? Glucagon



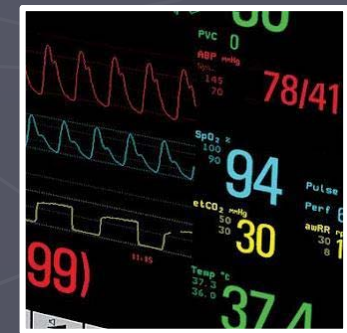
# Hemodynamic Effects of Methylene Blue

Methylene blue, a commonly used tissue marker, is normally hemodynamically inert.

However, for a variety of clinical scenarios associated with an inflammatory response, methylene blue results in increases of systemic blood pressure, systemic vascular resistance (SVR), and myocardial contractility.

The application of methylene blue's effects is also being studied in the management of numerous clinical scenarios, including:

- vasoplegia
- anaphylactic shock
- septic shock
- hypotension from ACE-Is/ARBs
- hemodialysis hypotension
- cardiogenic shock



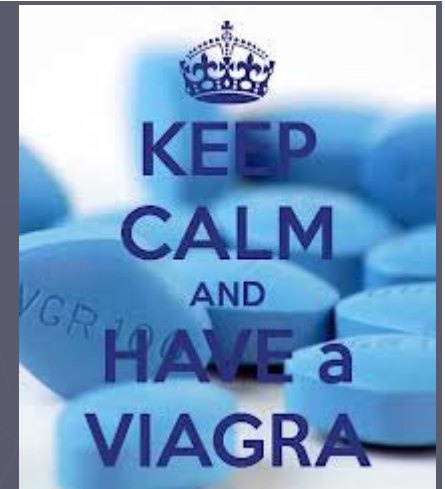
# Dosing of Vasopressin

## Intraoperative hypotension

- Dilute with 19 mL NS in a 20 cc syringe to create a concentration of 1 unit/mL.
- Administer 0.5 – 1 unit to treat hypotension in an adult.

## Septic Shock

- Exogenous vasopressin has been used in patients with septic shock in several studies. AVP infusion (0.01–0.04 U/min) increased peripheral vascular resistance and arterial blood pressure within minutes of application. No increase in pulmonary vascular resistance or pulmonary artery pressure was reported in patients treated with low-dose vasopressin (0.04 U/min), nor were cardiac complications or changes in electrolyte, blood and urine osmolality, or metabolic variables.



# Shortage

Reason for the Shortage American Regent discontinued vasopressin injection in early 2015.1,2 Par Sterile Products (formerly JHP) discontinued Pitressin injection in November 2014

Par Sterile Products introduced Vasostrict injection in November 2014. This is the only FDA-approved vasopressin injection.

Fresenius Kabi will discontinue distributing vasopressin on March 15, 2015. A letter is available regarding this discontinuation.

See more at:  
[http://www.ashp.org/menu/DrugShortages/CurrentShortages/bulletin.aspx?id=795#sth\\_ash.XkiyeTLH.dpuf](http://www.ashp.org/menu/DrugShortages/CurrentShortages/bulletin.aspx?id=795#sth_ash.XkiyeTLH.dpuf)

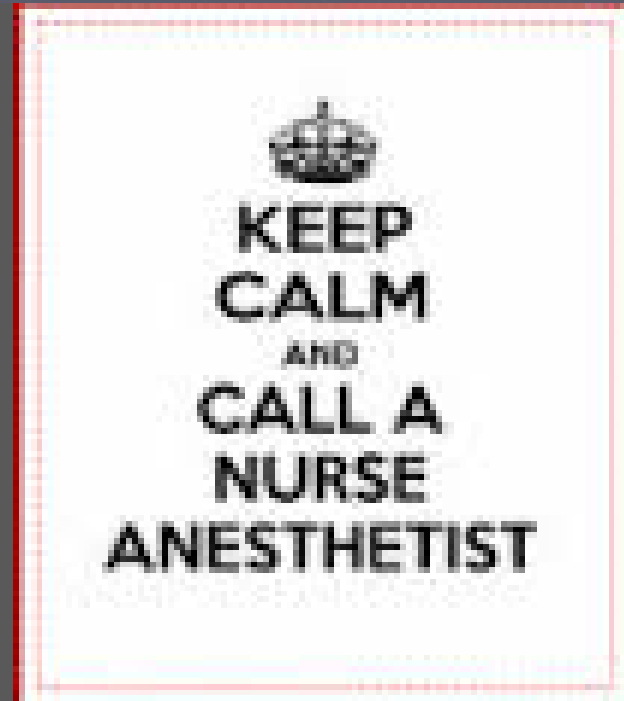
Available Products Vasostrict Injection, Par Sterile Products 20 units/mL, 1 mL multi-dose vial, 25 count (NDC 42023-0164-25)

See more at:  
[http://www.ashp.org/menu/DrugShortages/CurrentShortages/bulletin.aspx?id=795#sth\\_ash.XkiyeTLH.dpuf](http://www.ashp.org/menu/DrugShortages/CurrentShortages/bulletin.aspx?id=795#sth_ash.XkiyeTLH.dpuf)



# New Pain Drugs

- ▶ Ofirmev
- ▶ Caldolor
- ▶ Sufentanil Patch
- ▶ Nucynta
- ▶ Remoxy
- ▶ Mexiletine
  
- ▶ Antidote: Entereg
  - (almivopam)



# Multimodal Approach to Acute Pain Management



Severe Pain

**STEP 3**  
STEP 2  
*and*  
Higher doses of opioids

Moderate Pain

**STEP 2**  
STEP 1  
*and*  
Low doses of opioids

Mild Pain

**STEP 1**  
Acetaminophen, NSAIDs, or COXIBs  
*and*  
Local/regional anesthesia

Modified from Crews et al., 2002<sup>1</sup>

1. Crews JC. *JAMA*. 2002;288:629-632. 2. World Health Organization. Pain relief ladder. <http://www.who.int>. Accessed November 21, 2011. 3. Ventafridda V, et al. *Cancer*. 1987;59:850-856. 4. ASA Task Force. *Anesthesiology*. 2004;100:1573-1581.

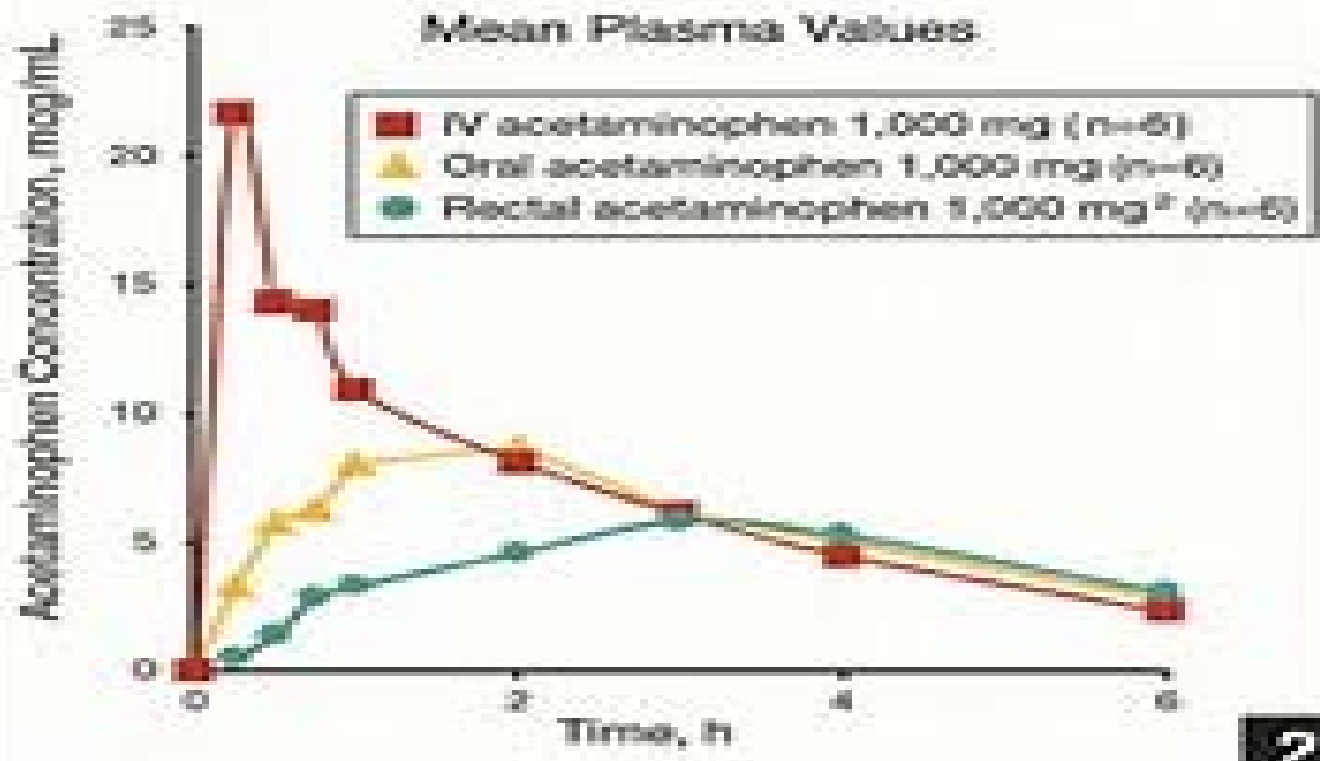
# OFIRMEV \$10.00/1000mg

- ▶ IV acetaminophen injection: Cadence Pharm
  - ▶ (Cadence was bought out) (price spike)
- ▶ Minimum dosing interval is every 4 hours
- ▶ Administer over 15 min.....well....?????
  - ▶ [www.ofirmev.com](http://www.ofirmev.com)
- ▶ Do not exceed max daily doses.. Adult is 4 grams per day
- ▶ Pediatric is dosed at 15mg/kg with max of 75 mg/kg/day



CHEAPPPPPPP-----Not any more... ???

- Regional Anesthesia Pain Management 2015 discusses that the purchase by Mallickrodt increased the price by 285%, costing the healthcare system nearly \$2.78 Million in inflation costs.



# OFIRMEV



- ▶ Liver issues is big
- ▶ Contraindicated in patients with liver failure/hepatic injury or with known hypersensitivity to acetaminophen...
- ▶ What about ETOH?
- ▶ Common side effects are: N/V; HA; insomnia; constipation, pruritus and agitation and atelectasis
- ▶ Using this drug may mask post surgical fever when used for post-operative pain.





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## COX-3: the Acetaminophen Target Finally Revealed

It has been known for years that non-steroidal anti-inflammatory drugs (NSAIDs) such as aspirin, ibuprofen, and acetaminophen, provide relief from fever, pain, and inflammation through their actions on cyclooxygenase (COX) enzymes.<sup>1</sup> Two COX isozymes, COX-1 and -2, were first identified in the early 1990's as the catalysts for an important step in prostaglandin biosynthesis.<sup>2</sup> Although both enzymes have similar functions, their temporal and spatial expression patterns are very different.<sup>3</sup> COX-1 is constitutively expressed in many somatic cell types and is considered a "housekeeping" enzyme with roles in such processes as vascular hemostasis and gastroprotection.<sup>4</sup> In contrast, COX-2 expression is primarily induced by factors such as endotoxins, cytokines, and growth factors.<sup>5</sup> COX-2 is expressed at sites of inflammation and produces prostaglandins that mediate inflammatory and pain sensation responses.<sup>6</sup> COX involvement in inflammation, pain, and a variety of diseases has inspired researchers to investigate the actions of NSAIDs on these enzymes. Although many advances have been made over the last 10 years in understanding the pain relief and anti-inflammatory mechanisms of aspirin, ibuprofen, and the new COX-2 inhibitors, the mechanism of acetaminophen action has remained elusive.<sup>7,8</sup>

Finally, identification of a new isozyme, COX-3, suggests that it is the target for acetaminophen.<sup>9</sup> COX-3 was discovered by Northern analysis of canine cerebral cortex RNA using a COX-1 cDNA probe. The COX-1 probe unexpectedly illuminated a band at 2.6 kb, labeling a transcript later confirmed to be COX-3, an alternate splice variant of COX-1 in which intron 1 is retained (Figure 1). Interestingly, intron 1 is not only present in canine, human, and murine versions of COX-3, but it is conserved in length and sequence in these species as well. While COX-3 retains all of the important catalytic and structural features of COX-1 and -2, it is likely that intron 1 is responsible for the deviant enzymatic properties of COX-3 perhaps via subtle alterations in structure, glycosylation state, and/or expression.<sup>9</sup>

Thus far, little is known about the temporal regulation of COX-3 expression. However, it has been known for decades that acetaminophen inhibits COX activity in canine brain



# Ibuprofen-Caldolor \$10



- ▶ Think about Ketorolac.. Actions and side effects
- ▶ Big differences... Less action on Cox 1 and more Cox 2 action..
- ▶ What does this mean? Less bleeding.. More pain control can give anytime during the surgery... better now that we can give per--op
- ▶ 400mg/4ml or 800mg/8ml
- ▶ Dilute and administer over 30 minutes
- ▶ 400mg-800mg Over 30 min repeat every 6 hours PRN\*
- ▶ Fluids “ well hydrated prior to use”



# Pain Control with a Old Drug?



Phantom pain... Calcitonin

Calcitonin is a 32 amino acid peptide hormone which regulates calcium homeostasis in vertebrates. It also has analgesic properties, primarily through receptor mediated modulation of serotonergic pain pathways in the central nervous system

A meta-analysis concluded that calcitonin was effective in the treatment of complex regional pain syndrome and systematic reviews reported benefit in the treatment of acute vertebral fracture pain. A randomized controlled trial (RCT) showed calcitonin was effective in the treatment of acute phantom limb pain, however a Cochrane review did not support its use in the treatment of metastatic bone pain although individual RCTs suggested benefit.

The drugs are aimed at a compound called calcitonin gene-related peptide or **CGRP**. Four different companies are testing drugs that affect CGRP: Alder Pharmaceuticals, Amgen, Eli Lilly and Company, and Teva Pharmaceuticals. CGRP is a neurotransmitter -- a message-carrying chemical.

ncbi.nlm.nih.gov/pubmed/26291126

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*Pain Res Manag.* 2015 Sep-Oct;20(5):229-33. Epub 2015 Aug 20.

**Use of calcitonin in recalcitrant phantom limb pain complicated by heterotopic ossification.**

Viana B, Payne MW.

**Abstract**

**BACKGROUND:** Phantom limb pain (PLP) is a common complication after amputation, affecting up to 80% of the amputee population. However, only 5% to 10% of amputees have severe PLP impacting daily function. The present report details the management of severe, treatment-resistant PLP in a 72-year-old man with a traumatic left transradial amputation and a comorbid complication of heterotopic ossification (HO).

**OBJECTIVE:** To describe a case of PLP with HO and the possible role of calcitonin in the treatment of both conditions.

**METHODS:** A systematic review of the literature regarding the management of PLP.

**RESULTS:** Seventeen articles that directly addressed PLP were identified; 11 were randomized controlled trials. All involved small samples and follow-up ranged from 6 h to one year, with the majority limited to six weeks.

**DISCUSSION:** In the present case, medication management was limited by side effects, lack of response and the patient's desire to avoid long-term medication. Investigations revealed HO, which was suspected to envelop the median nerve in the proximal forearm. After several unsuccessful medication trials, the literature was reviewed in search of common variables between HO formation and persistent PLP. Ultimately, the biochemical effects associated with nerve injury were identified to be a possible factor in both HO and PLP development. Calcitonin's proposed mechanisms of action may help to manage HO and PLP at multiple stages of disease development and maintenance. In the present case, a four-week trial of intranasal calcitonin was successful, with pain control lasting at least 18 months.

**CONCLUSION:** The present case report provided a review of the current literature in PLP pharmacological management and the current understanding of the etiology of PLP and HO, as well as how the two may coexist. It also provided an opportunity to discuss the proposed

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The contribution of sympathetic mechanisms to postamputation phantom and resid [J Pain. 2011]  
Review Calcitonin in phantom limb pain. [Ann Pharmacother. 1999]  
Calcitonin in phantom limb pain: a double-blind study. [Pain. 1992]  
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One or two  
doses of IV  
calcitonin  
200 IU

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*Curr Pharm Des.* 2003;9(32):2659-76.

**Calcitonin for osteoporosis and bone pain.**

Mehta NM<sup>1</sup>, Malootian A, Gilligan JP.

Author information

**Abstract**

Calcitonin has been approved for the treatment of osteoporosis and other diseases involving accelerated bone turnover for approximately 25 years. The most commonly studied and prescribed form is salmon calcitonin, which has a greater efficacy in clinical use. A wealth of well-controlled clinical studies have demonstrated that calcitonin preserves or increases bone mineral density (BMD) and reduces the risk of vertebral fractures in osteoporosis. Recent studies have indicated that while a low BMD is correlated with an increase in fracture risk, increases in BMD alone do not explain the antifracture efficacy of antiresorptive therapies such as calcitonin. Therapies that moderately increase BMD may reduce fracture risk by reducing the rate of bone turnover and maintaining the integrity of the trabecular architecture, resulting in the preservation of bone strength and quality in osteoporotic patients. An advantage of calcitonin that is not shared by other antiresorptive therapies is its direct analgesic effect on bone pain. Calcitonin has been demonstrated to be clinically useful in improving pain, not only from the acute vertebral fractures of osteoporosis, but also in Paget's disease, bone malignancies, and other sources of musculoskeletal pain. Drugs containing calcitonin may be approved for additional indications in the near future, and as more convenient routes of administration such as the oral route become available, the demand for the calcitonin peptide is expected to increase.

PMID: 14529539  
[PubMed - indexed for MEDLINE]

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Review Intranasal salcatonin (salmon calcitonin). A review of its ph [Drugs Aging. 1996]  
Review Salmon calcitonin: a review of current and future therapeutic indi [Osteoporos Int. 2008]  
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# Alkermes Pharm—Meloxicam IV

Meloxicam IV/IM is a proprietary, Phase III-ready, long-acting COX-2 NSAID used to target moderate to severe acute pain. Meloxicam IV/IM is a nonsteroidal anti-inflammatory drug... In five phase II studies treating more than 700 patients with acute pain, meloxicam IV/IM demonstrated positive effect on treating rapid onset of pain relief and "time to peak" analgesic effect, 18 to 24 hour duration of pain relief as well as favorable tolerability.



# Recro Pharm Dex-IN

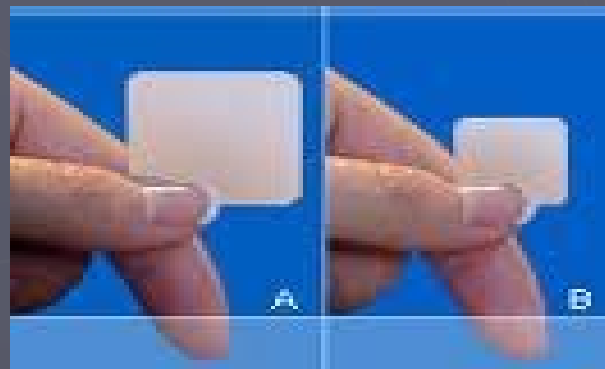
**Recro's** Dex-IN, an intranasal form of dexmedetomidine, which has been tested as an analgesic drug for post-operative pain. Last year the company's lead drug passed a Phase Ib trial that demonstrated its proof of concept in providing effective pain relief. However, in September **Recro Pharma** halted a trial of its lead product candidate Dex-IN.

The company decided to stop the trial because it does not believe the study would achieve "statistical significance" in its current design. **Recro Pharma** has an upcoming interim analysis of ongoing Post Op Day 1 Phase II trial for Dex-IN, and depending on clinical success, the possibility for two proprietary compounds to enter Phase III by year end.



# Sufentanil \$3.52/50mcg

- ▶ 5 - 10X more potent than fentanyl
- ▶ Sufentanil 0.0035 mg = fentanyl 0.05 mg
- ▶ Safe therapeutic index: 25,211
- ▶ Dose: .025 - 30  $\mu\text{g}/\text{kg}$
- ▶ Analgesic dose: 0.1 - 0.4  $\mu\text{g}/\text{kg}$  IV
- ▶ Maintenance dose: 1  $\mu\text{g}/\text{kg}$  followed by 0.25-0.5  $\mu\text{g}/\text{kg}/\text{hr}$
- ▶ High dose: 10 - 30  $\mu\text{g}/\text{kg}$



- ▶ **New PATCH coming out from Durrect Pharm....**

# Fentanyl Patch

- ▶ Transdermal Patch
- ▶ Technology changing for delivery
- ▶ **On Demand? : Fentanyl iontophoretic transdermal system provides a 40 mcg dose of fentanyl per activation on-demand**
- ▶ Other fentanyl thoughts:
  - ▶ BUCCAL TABLET; BUCCAL SOLUBLE FILM; SUBLINGUAL TABLETS; NASAL SPRAY; SUBLINGUAL SPRAY



# Fentanyl



**insYS**  
THERAPEUTICS, INC.

**SUBSYS**®  
(fentanyl sublingual spray)  
100, 200, 400, 600, 800, 1200, 1600 mcg

[www.subsyspray.com](http://www.subsyspray.com)



Not an actual Lazanda patient.

**Actiq**®  
(fentanyl citrate) oral  
transmucosal lozenge



Figure 2.



# The Patch!



**Clonidine produces a dose-dependent impairment of baroreflex-mediated thermoregulatory responses to positive end-expiratory pressure in anaesthetized humans**

Clonidine was clinically evaluated to suppress postoperative shivering in 60 patients who had undergone anesthesia for general, thoracic and vascular surgery. The study was carried out in double blind conditions with comparison of two doses (75 and 150 micrograms) of clonidine.

D3forME (Vitamin D3)

Catapres (clonidine)

Transderm (scopolamine)

Nicoderm (nicotine)

**Exelon (rivastigmine) possible muscle relaxant interaction ###**

Lidoderm (lidocaine)

Duragesic (fentanyl)

Fortesta, Axiron (testosterone)

Nitrodur (nitroglycerin)

Combipatch (estradiol, norethindrone) ? procoagulant

Alora, Menostar, Vivelle-dot, Estraderm (estradiol) ? procoagulant

Butrans (Buprenorphine) antagonizes opioids (mixed agonist/antagonist). Remove 4 days before surgery if need for significant doses of opioids postop

Emsam (selegiline = MAOI drug!) for severe depression or Parkinson's, may need to continue as long as providers



A Drug used for the treatment of Alzheimer's and is a cholinesterase inhibitor. Complete action is unknown!

Rivastigmine, an acetyl cholinesterase inhibitor, may be administered orally or as a transdermal patch for treatment of Alzheimer's disease and may interfere with neuromuscular blocking drugs.

Antibiotics

Renal Failure

Liver Failure

Temperature, Ph

Dibucaine Number

- ▶ FDA approves the first treatment for dementia of Parkinson's disease. FDA News Release. U.S. Food and Drug Administration. Available at: <http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2006/ucm108680.htm> Accessed October 16, 2013.
- ▶ Jeffrey S. FDA approves Exelon Patch for severe Alzheimer's. Available at: <http://www.medscape.com/viewarticle/807062> Accessed October 16, 2013.
- ▶ Baruah J, Easby J, Kessell G. Effects of acetyl cholinesterase inhibitor therapy for Alzheimer's disease on neuromuscular block. *Br J Anaesth* 2008;100:420.



# Microcron Technology Drugs---IROKO Pharm

ZORVOLEX is the first low dose FDA-approved NSAID developed using proprietary SoluMatrix Fine Particle Technology™.

**ZORVOLEX contains diclofenac as submicron particles that are approximately 20 times smaller than their original size. The reduction in particle size provides an increased surface area, leading to faster dissolution.**

ZORVOLEX was developed to align with recommendations from FDA and other professional medical organizations that NSAIDs be used at the lowest effective dose for the shortest possible duration consistent with individual patient treatment goals. For more information, visit [www.zorvolex.com](http://www.zorvolex.com).

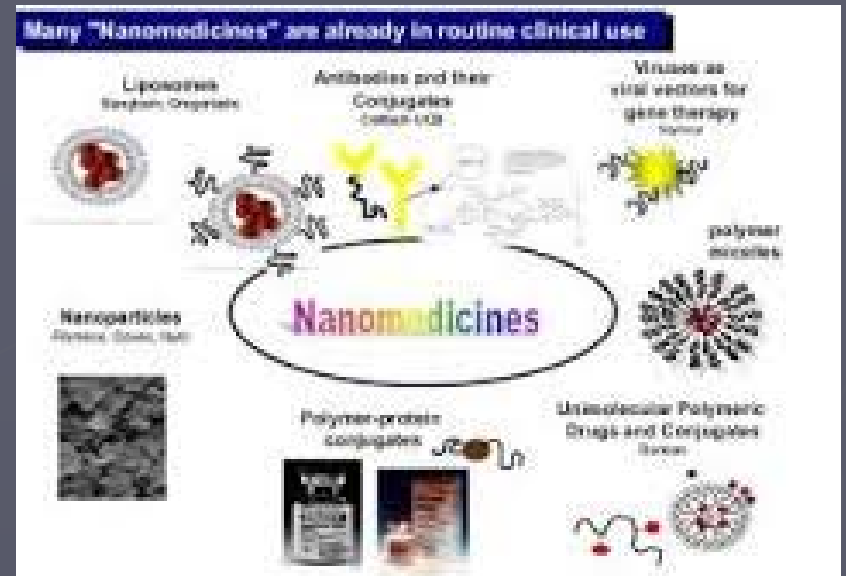


# Nanoparticles:

Recent article:

**Nano anesthesia: A Novel, Intravenous Approach to Ankle Block in the Rat by Magnet-Directed Concentration of Ropivacaine-Associated Nanoparticles**

**Anesthesia and Analgesia: April 2014**



# Exparel

- ▶ EXPAREL is a local analgesic that utilizes bupivacaine in combination with the proven product delivery platform, DepoFoam®. A single intraoperative injection given at the close of surgery delivers postsurgical pain control with reduced opioid requirements for up to 72 hours
- ▶ Following its release from the DepoFoam® particles, the rate of systemic absorption of bupivacaine is dependent upon the total dose of drug administered, the route of administration, and the vascularity of the administration site

a pivotal soft tissue trial of EXPAREL versus placebo, patients experienced a 30% reduction in cumulative pain scores and a 45% reduction in opioid consumption



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Silver Spring, MD 20993

**TRANSMITTED BY FACSIMILE**

Dave Stack  
President and CEO  
Pacira Pharmaceuticals, Inc.  
5 Sylvan Way  
Parsippany NJ 07054

**RE: NDA # 022496**  
EXPAREL® (bupivacaine liposome injectable suspension)  
MA# 68

**WARNING LETTER**

Dear Mr. Stack:

As part of its routine monitoring and surveillance program, the Office of Prescription Drug Promotion (OPDP) of the U.S. Food and Drug Administration (FDA) has reviewed educational technique flashcards (EXP-AP-0124-201209 & EXP-AP-0134-201210) (administration guides) and a journal ad (EXP-AP-0039-201302) for EXPAREL® (bupivacaine liposome injectable suspension) (Exparel) submitted by Pacira Pharmaceuticals, Inc. (Pacira) under cover of Form FDA-2253. The journal ad was also submitted as a complaint to the OPDP Bad Ad Program. The administration guides provide evidence that Exparel is intended for new uses for which it lacks approval, and for which its labeling does not provide adequate directions for use, which renders Exparel misbranded within the meaning of the Federal Food, Drug, and Cosmetic Act (FD&C Act), and make its distribution violative. See 21 U.S.C. 355(a), 352(f); 331(a), (d); 21 CFR 201.5; 201.100; 201.115; 201.128. In addition, the journal ad is false or misleading because it overstated the efficacy of Exparel. The journal ad



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- In Memoriam
- National CRNA Week
- Current Events
- Convention Daily

[AANA](#) / [News & Journal](#) / [News](#)

## Potential for Wrong Route Errors with Exparel

There is a dangerous potential for errors in the administration of two "look-alike" medications that are or will be common in anesthesia practice in this country: propofol and the new bupivacaine liposomal suspension Exparel, *not meant for IV administration*. Both are milky white suspensions, and because propofol has been the only such medication for many years, a real potential for error exists.

Exparel is a local anesthetic that is infiltrated into a surgical wound during a surgical procedure to produce postsurgical analgesia. It is not intended for systemic use. When prepared in syringes, these products essentially look identical. If Exparel is accidentally administered intravenously instead of propofol, *toxic blood concentrations might result, and cardiac conductivity and excitability may be depressed, which may lead to atrioventricular block, ventricular arrhythmias, and cardiac arrest.*

Propofol is used as an anesthetic during surgical procedures and as a sedative during procedures or for patients undergoing mechanical ventilation. Thus, Exparel and propofol may be used in similar healthcare settings.

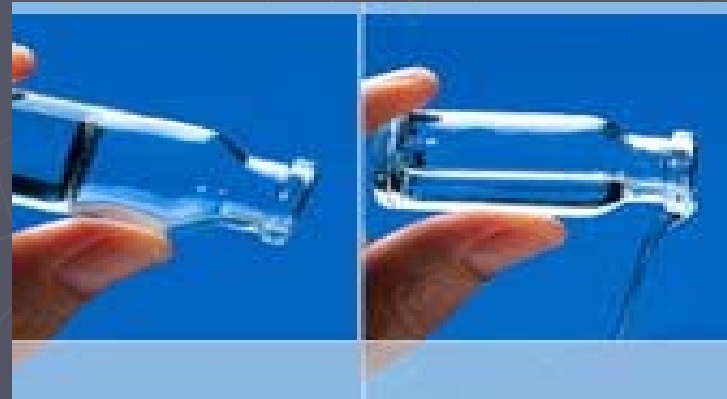
Read more: [MAY 11, 2016](#)

# Exparel



# Posidur

- ▶ New product just like Exparel
- ▶ Except Clear.... Could this be trouble?



# Lipid Rescue

## ▶ 20% lipid solution

▶ 1.5 ml/kg over 1 minute

▶ Follow immediately by a infusion at rate of 0.25ml/kg/min  
(17.5 ml/min for a 70 kg adult)

▶ Repeat dose if no improvement – and double the infusion rate

▶ Max of 10 ml/kg???

▶ [www.lipidrescue.org](http://www.lipidrescue.org)

▶ ACLS-----limit epi----Weinberg work!

▶ What about Propofol? (Propofol is 1%)



## LipidRescue™

### TREATMENT FOR LOCAL ANESTHETIC-INDUCED CARDIAC ARREST

**PLEASE KEEP THIS PROTOCOL ATTACHED TO  
THE INTRALIPID BAG**

In the event of local anesthetic-induced cardiac arrest that is unresponsive to standard therapy, in addition to standard cardio-pulmonary resuscitation, Intralipid 20% should be given i.v. in the following dose regime:

- Intralipid 20% 1.5 mL/kg over 1 minute
- Follow immediately with an infusion at a rate of 0.25 mL/kg/min,
- Continue chest compressions (lipid must circulate)
- Repeat bolus every 3-5 minutes up to 3 mL/kg total dose until circulation is restored
- Continue infusion until hemodynamic stability is restored. Increase the rate to 0.5 mL/kg/min if BP declines
- A maximum total dose of 8 mL/kg is recommended

*In practice, in resuscitating an adult weighing 70kg:*

- Take a 500ml bag of Intralipid 20% and a 50ml syringe.
- Draw up 50ml and give stat i.v., X2
- Then attach the intralipid bag to an iv administration set (macro drip) and run it i.v. over the next 15 minutes
- Repeat the initial bolus up to twice more – if spontaneous circulation has not returned.

If you use Intralipid to treat a case of local anaesthetic toxicity, please report it at [www.lipidrescue.org](http://www.lipidrescue.org). Remember to restock the lipid. Ver 7/06



# Mivacurium is coming back...

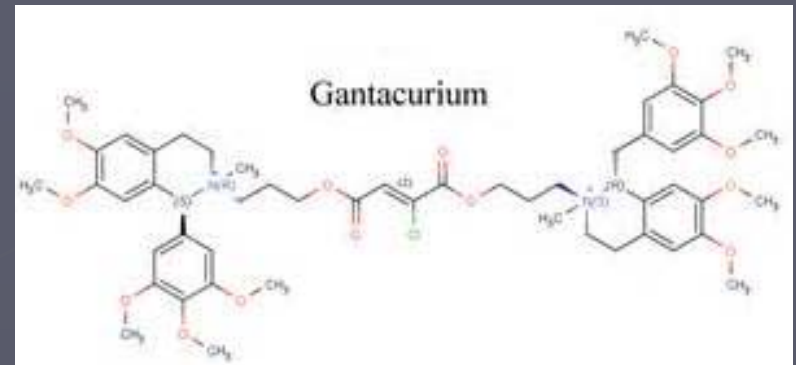
The screenshot shows a web browser window with the URL `marketresearch.com/Prof-Research-v4036/Mivacurium-CAS-10268432`. The page features a blue header with the Market Research.com logo and navigation links. Below the header, a breadcrumb trail reads: `Heavy Industry » Manufacturing & Construction » Manufacturing » Chemical Manufacturing`. The main heading is `2016 Mivacurium (CAS 106791-40-6) Industry Market Report`. A table of specifications is displayed:

Lowest Prices Guaranteed	Length	Publisher	Published Date	SKU
from \$2,900	150 Pages	Prof-Research	August 30, 2016	PROF15093369

Below the table are buttons for `Table of Contents` and `Description`. At the bottom, there is a `Purchase` button for \$2,900, a `Research assistance` button, and a `PDF E-mail From Publisher` link. A vertical `Feedback` button is on the right side of the page. The Windows taskbar at the bottom shows the date as 9/23/2016 and the time as 3:25 PM.

# Gantacurium

## Phase 2 complete



- ▶ Is this a new Generation being born of NMB?
- ▶ Based on amino acid pathway—**olefinic**
- ▶ This drug is chemically degraded by rapid adduction to L-cysteine and removes Chlorine
- ▶ These two routes make it unavailable to bind to acetylcholine receptor
- ▶ Does not require Liver, Kidneys, Temperature or pH
- ▶ Two exciting analogs...
- ▶ There has always been a search for the new Succx.....

# Gantacurium

- ▶ Dose: 0.5 mg/kg
- ▶ Fast acting with short duration
- ▶ Exciting new group of drugs!
- ▶ Key is: NO histamine release!

# CW002

- ▶ Same pathway as Gantacurium!
- ▶ This compound Lacks Chlorine
- ▶ Dose: 0.15mg/kg
- ▶ Fast acting Intermediate duration
- ▶ Key is: NO histamine release!

# CW 011

- ▶ This is the baby of this group...
- ▶ Lacks Chloride so slower to break down
- ▶ Dose: 0.10 mg/kg
- ▶ Fast acting more intermediate duration
- ▶ Key is: NO histamine release!

# L-Cysteine

Dissolved in concentration of 200mg/ml

- ▶ Antidote for New class of Muscle relaxants
  - Olefinic isoquinolone Diester NMB
  - Only works with new group of NMB's

The screenshot shows a web browser displaying the ASA Publications website. The page features a teal header with the ASA logo and navigation links. The main content area displays an article titled "Rapid Chemical Antagonism of Meeting Abstracts by L-Cysteine Adduction to and Inactivation of the Olefinic (Double-bonded) Isoquinolinium Diester Compounds Gantacurium (AV430A), CW 002, and CW 011". The article is marked as "FREE" and is from the July 2010 issue of "Anesthesiology". The authors listed are John J. Savarese, M.D.; Jeff D. McGilvra, Ph.D.; Hiroshi Sunaga, M.D.; Matthew R. Belmont, M.D.; Scott G. Van Ornum, Ph.D.; Peter M. Savard, M.D.; and Paul M. Heerd, M.D., Ph.D. To the left of the article is a thumbnail for the journal cover, and to the right is a "RELATED ARTICLES" section with several titles. The browser's address bar shows the URL "anesthesiology.pubs.asahq.org/Article.aspx?articleid=1933133". The Windows taskbar at the bottom shows the time as 3:29 PM on 9/23/2016.

# Cysteine

Human Studies: IV administration of exogenous L-Cysteine induced faster recovery.

Dose in Studies: 5-50mg/kg

- (average dose is 10mg/kg)

Compared to Edrophonium reversal with atropine.

Did not need to give antimuscarinics agent.

Reversed in 1 minute

There are risks...High doses: (added to TPN) but 1-1.5 grams/kg can cause neuro defects reported in infants



# apsf NEWSLETTER

February 2016

### Articles:

[Monitoring of Neuromuscular Blockade](#)

[Large Anesthesia/Practice Management Groups](#)

[Expanding Our Influence](#)

[President's Report](#)

[Safety of Neuromuscular Blockade](#)

[History of Sugammadex](#)

[Emergency Manual Workshop](#)

[FDA Issues Drug Safety Communication](#)

[NMB Reversal and Outcomes](#)

[Q&A:OR Power Failure](#)

[Dear SIRS: Incorrect Network Connection](#)

**Announcements:**  
[Save the Date](#)

[Merck Support of APSF](#)

[NBCRNA Support of Grant](#)

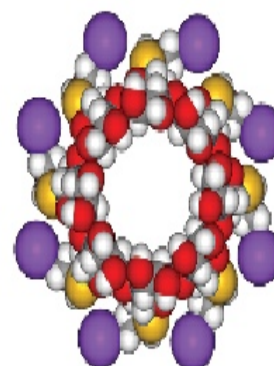
[Medtronic Support of APSF](#)

[APSF DVDs](#)

## The Development and Regulatory History of Sugammadex in the United States

by Glenn Murphy, MD

The Neuromuscular Research Group at Organon Newhouse Scotland (east of Glasgow) had been working on the development of fast-onset, short-acting, nondepolarizing steroidal neuromuscular blocking agents since the 1960s, which led to the development of pancuronium, vecuronium and rocuronium. Shortly after the launch of rocuronium, questions arose about a possible action of rocuronium on smooth muscle neurotransmission, so Dr. Anton Bom was contacted. Dr. Bom was



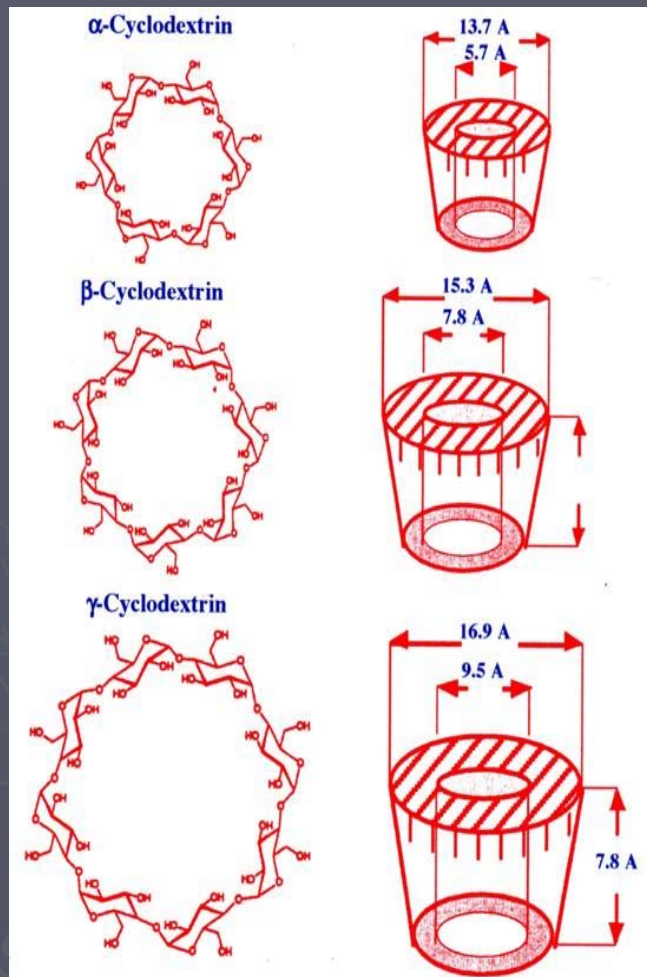
Dr. Anton Bom (own work) [Public domain, via Wikimedia Commons]

Space-filling model of sugammadex sodium.

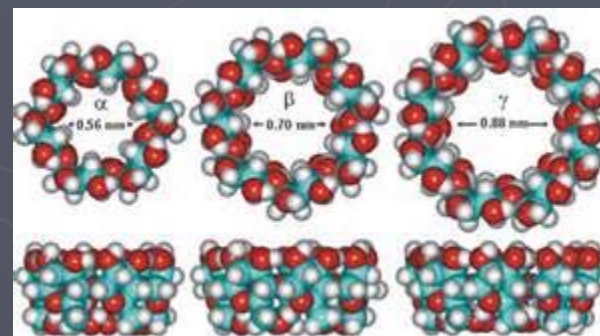
performing smooth muscle studies at the same research site. Rocuronium is not very water soluble, so buffer solutions with a pH of 4 are required. Dr. Bom attempted to dissolve rocuronium in organic solvents that were traditionally used for smooth muscle studies, none of which were able to solubilize rocuronium. Next, he decided to examine cyclodextrins, which were demonstrated to dissolve steroidal hormones. Cyclodextrins are rigid, ring-shaped molecules composed of sugar units. The outside of the cyclodextrin is hydrophilic, which makes the molecule water-soluble. The hole in the middle of the cyclodextrin ring is hydrophobic, which allows lipophilic molecules, like steroids, to enter this cavity, creating water-soluble complexes.<sup>1</sup>

Since rocuronium has a steroidal nucleus, Dr. Bom speculated that rocuronium would form complexes with cyclodextrins. This binding would prevent rocuronium from acting on the nicotinic acetylcholine receptor and allow rapid reversal of neuromuscular

# CYCLODEXTRINS



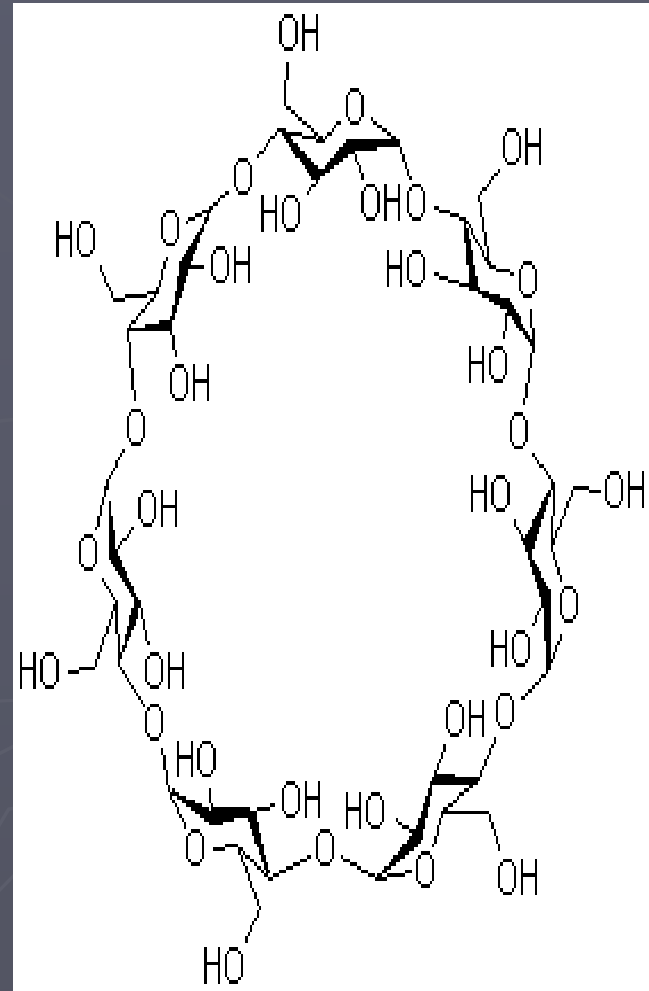
Cyclodextrins are poly saccharide compounds that were analyzed as scavenging molecules for toxins and additives for food materials



Beta Cyclodextrins were developed as vehicles for long acting drugs

They have been tried as solubilizing agents for various drugs like

Propofol, bupivacaine,  
sufentanil



# Sugammadex--Bridion



- ▶ 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 mis-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



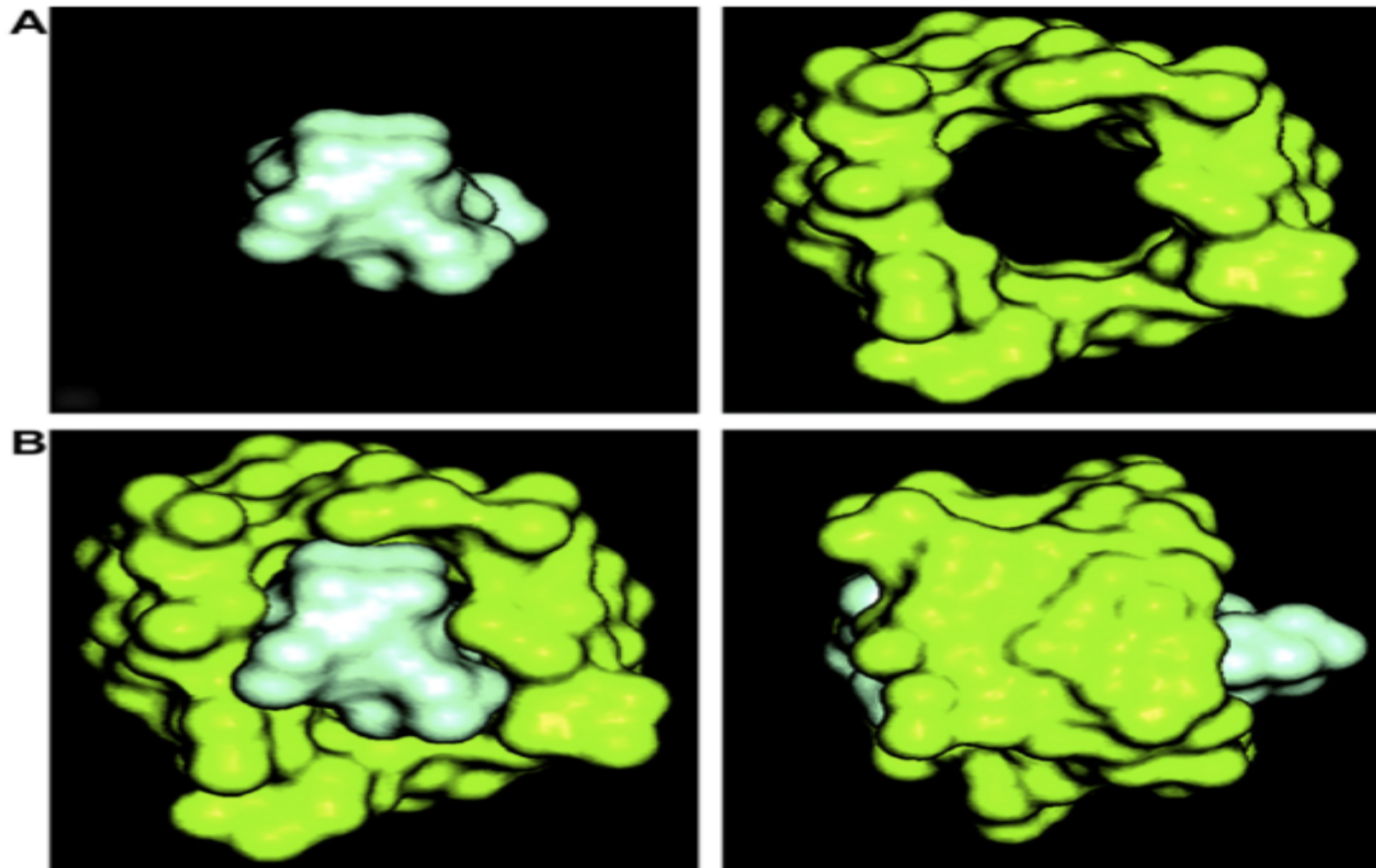
- ▶ Does not affect SUXX or benzylisoquinoliniums;
- ▶ If after using Sugammadex and paralysis needs to be achieved consider using these drugs
- ▶ SIDE EFFECTS: hypotension; coughing (was from a study when given to awake patients) vomiting, nausea, dry mouth, decreased temperature
- ▶ Is traditional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

# Cost of Sugammadex

- ▶ 70kg man
- ▶ 2mg/kg dose: 140mg, one 2mL vial = \$84.93
- ▶ 4mg/kg dose: 280mg, one 5mL vial = \$155.55
- ▶ 16mg/kg dose: 1120mg, two 5mL vials and one 2mL vial = \$396.03
- ▶ Caveats
  - Uncontracted prices from distributor
  - Patient cost usually approximately 3x this cost

Dose examples: ROC 1.2mg.kg administered and three minutes later 16mg/kg of Sugammadex given, this provides faster onset/offset profile than suxx

Will this change the face of anesthesia??



**Fig. 5.** (A) Current Radiograph crystal structure of a rocuronium molecule and a sugammadex molecule. (B) Synopsis encapsulation of rocuronium molecule (*blue*) by a sugammadex molecule (*green*) at 1:1 ratio. (From Cameron KS, Clark JK, Cooper A, et al. Modified gamma-cyclodextrins and their rocuronium complexes. *Org Lett* 2002;4:3403–6 ©American Chemical Society; with permission.)

Source: Full Prescribing Information, Bridion® (Sugammadex). 2015, Merck Sharpe and Dohme Corp. Akha AS et al. Sugammadex: Cyclodextrins, Development of Selective Binding Agents, Pharmacology, Clinical Development, and Future Directions. *Anesthesiology Clin* 28 (2010) 691-708

# Sugammadex - FDA Saga

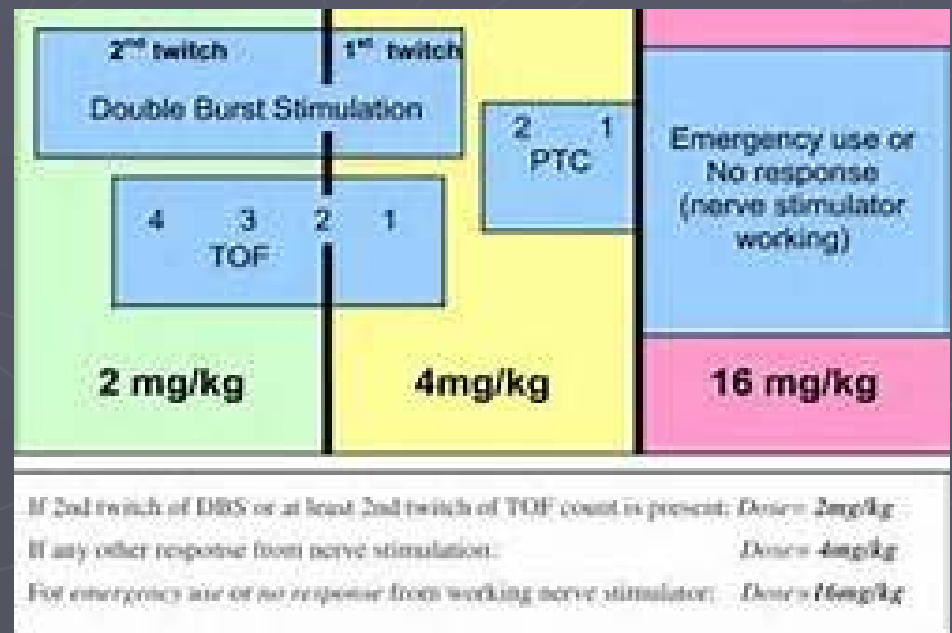
2014 Lit review identified 15 cases of hypersensitivity reactions from sugammadex.

All within 5 minutes of administration.  
Most common reactions rash and anaphylaxis.

11 patients skin tested, 10 positive

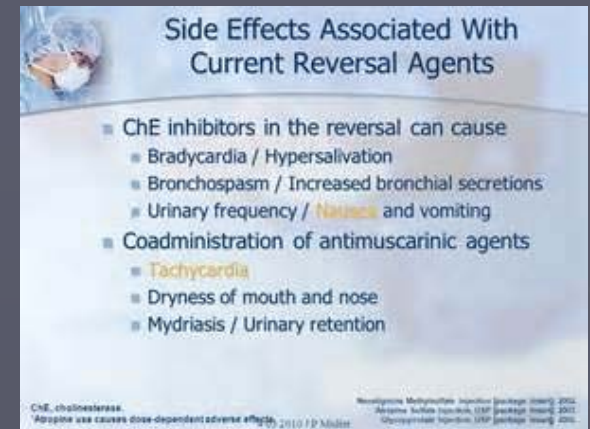
# Use of Sugammadex

- ▶ Binds Roc > Vec >> Panc
- ▶ Dose Depends on Depth – Single Bolus
  - If 2 TOF twitches returned, **2mg/kg**
  - If 1-2 PTC and 0 TOF twitches, **4mg/kg**
  - If reversal needed as soon as 3 mins after 1.2mg/kg rocuronium dose, **16mg/kg**
- ▶ Confirm reversal
- ▶ Time = 1.5-3 minutes (mean)



# Sugammadex – Adverse Reactions

- ▶ Serious but rare:
  - Anaphylaxis
  - Bradycardia
- ▶ > 10%
  - Nausea, Vomiting, Pain, Hypotension, Headache
- ▶ Signs of emergence (moving, sucking, chewing)
- ▶ Large meta-analysis with > 1500 patients = no significant difference in side effects compared with neostigmine with less residual paralysis





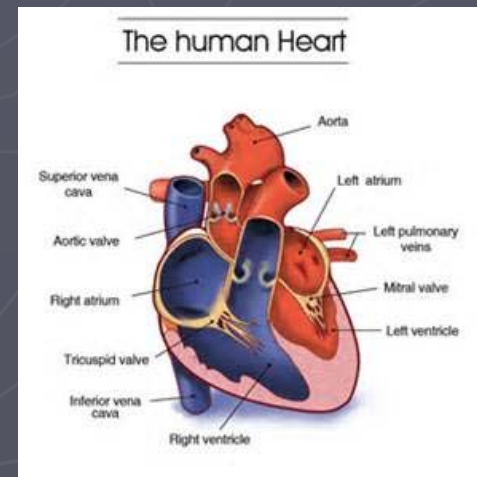
# Sugammadex - Bleeding

- ▶ Increases PTT, PT/INR up to 25% for up to 1h in healthy volunteers
- ▶ In a study of patients with major lower extremity orthopedics surgery, PTT and PT/INR increases < 10% were noted (**did NOT require transfusion**)
- ▶ No difference in bleeding, anemia incidence
- ▶ Concomitant thromboprophylaxis in this study

# Cardiac

In order to address concerns related to cardiac arrhythmias, an analysis of phase 2 and 3 clinical studies was conducted, as well as an analysis of post-marketing data.

These study findings indicated that QTc was not prolonged in patients given sugammadex. The studies also indicated that arrhythmias did not occur with greater frequency with sugammadex compared to neostigmine, although bradycardia can occur with both agents.



# Sugammadex – Not For Use In

- ▶ Children < 18
  - Some rat studies show possible decreased bone development in childhood
- ▶ Severe renal impairment (renal excretion)
  - GFR < 30
- ▶ Elderly patients exhibit slower recovery

# Sugammadex - Bleeding

- ▶ Increases PTT, PT/INR up to 25% for up to 1h in healthy volunteers
- ▶ In a study of patients with major lower extremity orthopedics surgery, PTT and PT/INR increases < 10% were noted
- ▶ No difference in bleeding, anemia incidence
- ▶ Concomitant thromboprophylaxis in this study

# Sugammadex – Drug Interactions

- ▶ Toremifene (SERM) may prolong NMBD recovery
- ▶ Other drugs could displace rocuronium
- ▶ Physically incompatible with: **ondansetron**, ranitidine, verapamil

# FDA Warns!

FDA also warned about the potential for marked bradycardia, and that some of these cases have resulted in cardiac arrest, often within minutes of giving the drug.

Patients should be closely monitored for hemodynamic changes during and after reversal of neuromuscular blockade, and physicians should give anticholinergic agents, such as atropine, if they observe clinically significant bradycardia, the agency said.

Physicians should also advise women using hormonal contraceptives that the drug may temporarily reduce contraceptive efficacy, so they should use an alternative method of birth control for a period of time after getting the drug.

The most common adverse reactions with sugammadex included vomiting, hypotension, pain, headache, and nausea.

# Recurarization Bottom Line

- ▶ (Except in magnesium case) No clinically significant recurarization has been reported when sugammadex is used as labeled according to manufacturer recommendations
- ▶ Recurarization can be seen if an inadequate dose is used!!

# Package insert

**Merck:**

## **7.3 Interaction Potentially Affecting the Efficacy of Hormonal Contraceptives**

*In vitro* binding studies indicate that BRIDION may bind to progestogen, thereby decreasing progestogen exposure. Therefore, the administration of a bolus dose of BRIDION is considered to be equivalent to missing dose(s) of oral contraceptives containing an estrogen or progestogen. If an oral contraceptive is taken on the same day that BRIDION is administered, the patient must use an additional, non-hormonal contraceptive method or back-up method of contraception (such as condoms and spermicides) for the next 7 days.

In case of non-oral hormonal contraceptives, the patient must use an additional, non-hormonal contraceptive method or back-up method of contraception (such as condoms and spermicides) for the next 7 days.

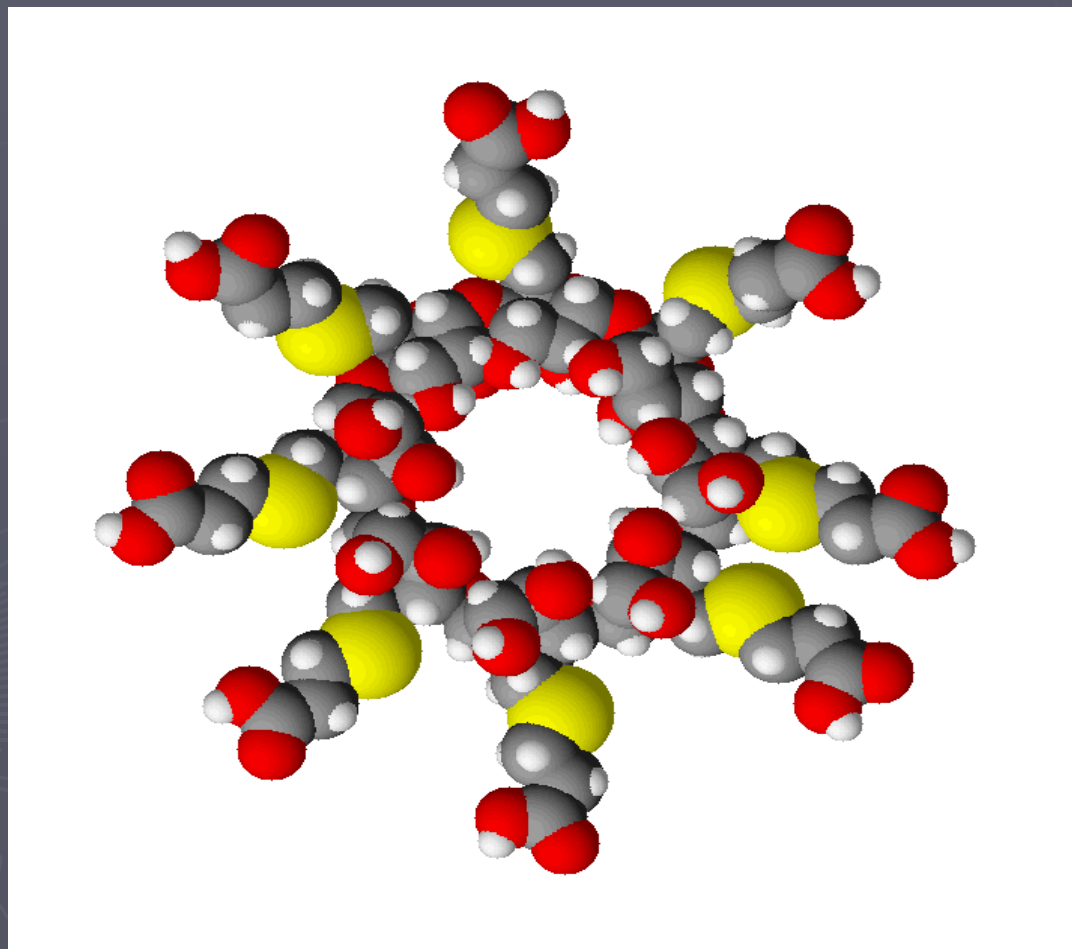
# Always Aware

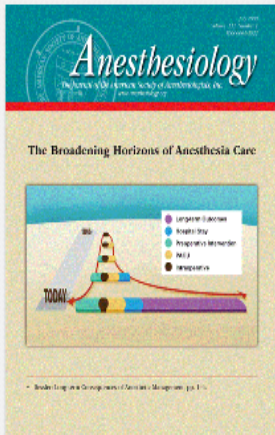
## **Sugammadex and Hormonal Birth Control Interaction: Identifying and Educating Affected Patients Automatically through Health Link**

Sugammadex is a medication indicated for the rapid reversal of neuromuscular blockade induced by rocuronium and Vecuronium. It was recently added to the formulary and is restricted to use in the OR and ED. Sugammadex interacts with hormonal birth control, both oral and non-oral formulations, possibly resulting in temporary loss of efficacy of the birth control for up to seven days.

Beginning September 13, 2016 documentation of sugammadex administration by the provider will generate an automatic educational message for women of reproductive potential who are between the ages of 10 and 60 years old. The message informs them that they received sugammadex. It also provides information about the nature of the interaction and the need for back-up birth control for seven days. Condoms and spermicides are recommended.

# Sugammadex





View Full Size

ISSUE

- Methods and Materials
- Results
- Discussion
- References

FREE

Perioperative Medicine | July 2009

## Preoperative Melatonin and Its Effects on Induction and Emergence in Children Undergoing Anesthesia and Surgery

Zeev N. Kain, M.D., M.B.A.; Jill E. MacLaren, Ph.D.; Leslie Herrmann, B.S.; Linda Mayes, M.D.; Abraham Rosenbaum, M.D.; Justin Hata, M.D.; Jerrold Lerman, M.D., F.R.C.P.C., F.A.N.Z.C.A.

+ Author Affiliations & Notes

Anesthesiology 7 2009, Vol.111, 44-49.  
doi:10.1097/ALN.0b013e3181a91870

### RELATED ARTICLES

- Sevoflurane versus Halothane: Postoperative Maladaptive Behavioral Changes: A Randomized, Controlled Trial
- Family-centered Preparation for Surgery Improves Perioperative Outcomes in Children: A Randomized Controlled Trial
- The Clinical Anaesthesia Viva Book, 2nd Edition.
- Changes in Functional Residual Capacity and Lung Mechanics during Surgical Repair of Congenital Heart Diseases: Effects of Preoperative Pulmonary Hemodynamics

# Antidote to Factor X inhibitors

Portola Pharmaceuticals (Nasdaq:[PTLA](#)) today announced that **andexanet alfa**, a U.S. Food and Drug Administration (FDA)-designated breakthrough therapy, has been granted orphan drug designation by the FDA's Office of Orphan Products Development for reversing the anticoagulant effect of direct or indirect Factor Xa inhibitors in patients experiencing a serious uncontrolled bleeding event or who require urgent or emergent surgery. Currently, there is no approved antidote for these patients.

**Praxbind (idarucizumab)** for use in patients who are taking the anticoagulant Pradaxa (dabigatran) during emergency situations when there is a need to reverse Pradaxa's blood-thinning effects.

Trial included 123 patients taking Pradaxa who received Praxbind due to uncontrolled bleeding or because they required emergency surgery. In this ongoing trial, based on laboratory testing, the anticoagulant effect of Pradaxa was fully reversed in 89 percent of patients within four hours of receiving Praxbind. In this patient trial, the most common side effects were low potassium (hypokalemia), confusion, constipation, fever and pneumonia.



# Others that might impact Anesthesia

- ▶ JM-1232 New hypnotic nonbenzo from Japan
- ▶ PF0-713 Variant of Propofol
- ▶ AZD-3043 Nonbarb hypnotic

**Just FDA approved:**

**Idarucizumab to reverse pradaxa**

**Factor X concentrate**

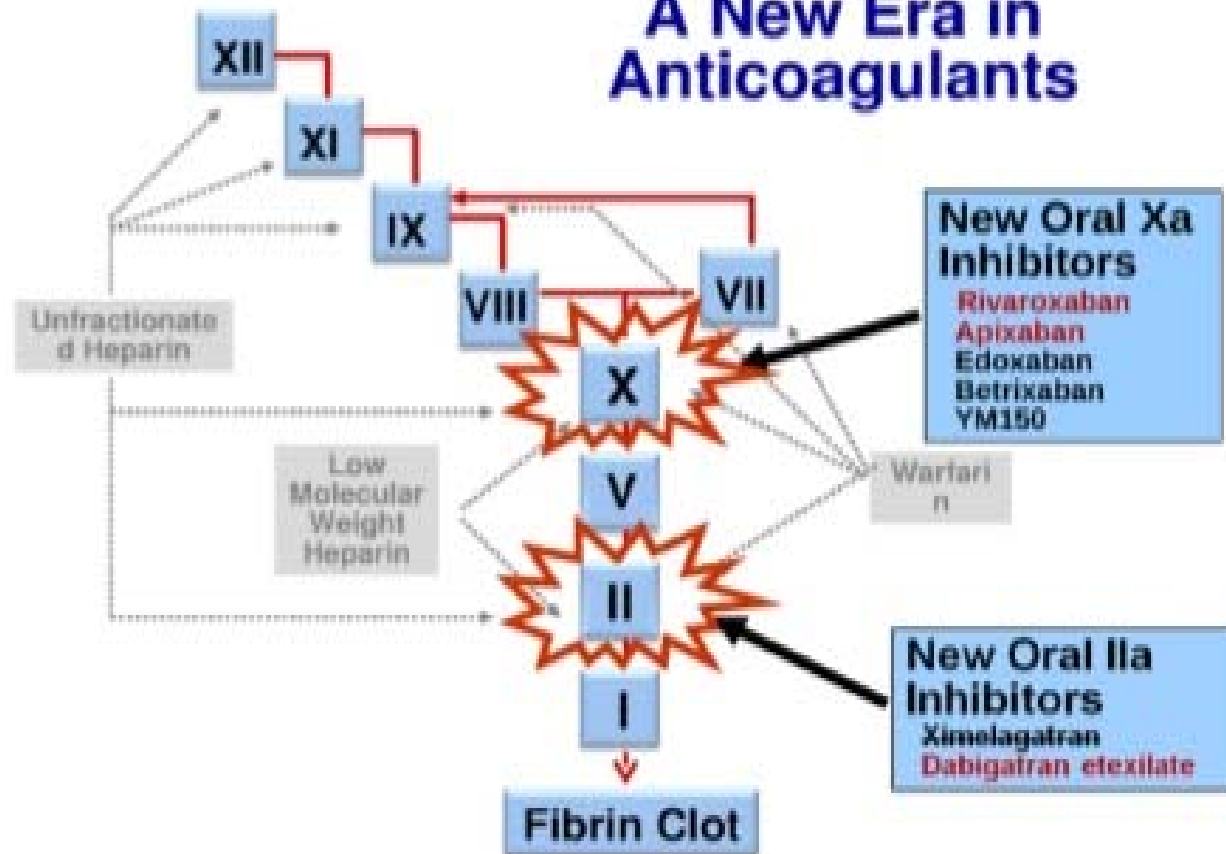


**RE-VERSE AD™**

Study of reversal effects of idarucizumab  
in patients on active dabigatran

# Mechanism of action

## A New Era in Anticoagulants



# Questions

Thank you!

Email me for the articles:  
[pstrube3000@yahoo.com](mailto:pstrube3000@yahoo.com)

