Regional Anesthesia Update 2014

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Disclosures

I have no commercial conflicts of interest

Objectives

1. Discuss the clinical applications and potential future directions of liposomal bupivacaine
2. Review the current literature regarding dexmedetomidine and regional anesthesia
3. Discuss the implications of regional anesthesia in patients with documented or suspected obstructive sleep apnea
4. Compare the effects of adductor canal blockade versus femoral nerve blockade in the management of patients undergoing total knee arthroplasty
5. Recognize the novel anticoagulants in clinical use and discuss the recent and potential modifications to the ASRA consensus guidelines concerning regional anesthesia and anticoagulation

PERIPHERAL NERVE BLOCKS

Do Peripheral Nerve Blocks Last Long Enough?

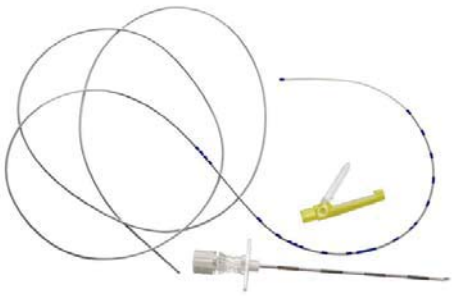
Are Patients Satisfied After Peripheral Nerve Blockade? Results From an International Registry of Regional Anesthesia

Craig M. Ironfield, MB, BS, BMedSci, Michael J. Barrington, MB, BS, FANZCA, PhD,*† Roman Kluger, MB, BS, FANZCA, MBiostat,* and Brian Sites, MD‡*

Physical complaints were common, **especially pain after surgery and particularly pain after [peripheral nerve block] recession.** Moderate or severe complaints of motor weakness were associated with unwillingness to undergo repeat PNB. Patients who reported severe symptoms in response to any of the questions in the pain domain were less willing to undergo repeat PNB

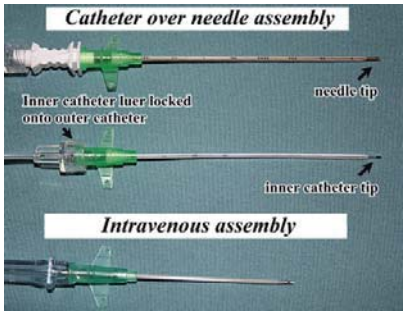
Reg Anesth Pain Med 2014;39: 48–55

Peripheral Nerve Catheter



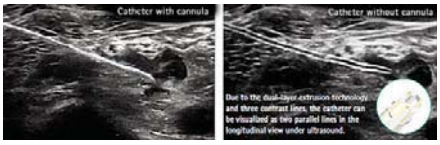
www.mycolumbiaasia.blogspot.com

Catheter-Over-Needle (Pajunk)



Can J Anaesth. 2013 Jul;60(7):692-9

Catheter-Over-Needle (B|Braun)



www.bbraunusa.com

Perineural Catheter Toxicity

Serum Free Ropivacaine Concentrations Among Patients Receiving Continuous Peripheral Nerve Block Catheters: Is It Safe for Long-Term Infusions?

Lisa Bleckner, MD,*§ Che Solla, MD,* Bader B. Fileta, BS,† Robin Howard, MA,† Carlos E. Morales, BS,§ and Chester C. Buckenmaier, MD*§

CONCLUSIONS: In this study, free serum ropivacaine concentrations remained well below toxic values despite large amounts of drug administration in combat-wounded patients. The administration of continuous ropivacaine infusions over prolonged time periods, coupled with multiple drug boluses, did not produce toxic or near-toxic serum concentrations. (Anesth Analg 2014;118:225–9)

Pediatric Ambulatory Perineural Catheters

Ambulatory Continuous Peripheral Nerve Blocks in Children and Adolescents: A Longitudinal 8-Year Single Center Study

Harshad Gurnaney, MBBS, MPH, F. Wickham Kraemer, MD, Lynne Maxwell, MD, Wallis T. Muhly, MD, Laura Schleelein, MD, and Arjunan Ganesh, MBBS

BACKGROUND: Although the role of regional anesthesia in pediatric patients has been increasing over the last few years, there are only a few small case series that describe the use of ambulatory continuous peripheral nerve blocks (CPNBs) in this patient population. In this report, we describe our experience with the use of ambulatory CPNBs in 1285 children.
METHODS: Data were collected for consecutive children who had a CPNB placed between January 2005 and December 2011 at The Children's Hospital of Philadelphia from the departmental regional anesthesia database. Data collected included demographics, the site of catheter placement and technique of nerve block, presence of sensory/motor blockade, use of perioperative opioids, and any complications related to CPNBs.
RESULTS: Continuous infusions of local anesthetics were administered via the catheters in 1285 outpatients. The mean duration of the CPNB was 50.7 ± 14.4 hours (mean ± SD). Among patients discharged home with the CPNBs, 969 (75.4%) of the patients required either no supplemental opioids or oral opioids only on an "as needed" basis in the postoperative period (confidence interval, 73.0%–77.8%). Two patients were readmitted for IV pain management after they were discharged home with the CPNB catheters. No neurological deficit related to the CPNBs was identified in any of the patients at their 6-month follow-up with the orthopedic surgeon (confidence interval, 0%–0.29%).
CONCLUSION: This audit of 1285 children shows ambulatory CPNBs can provide postoperative analgesia and may reduce the need for inpatient parenteral opioid therapy. (Anesth Analg 2014;XXX:00–00)

Perineural Catheter Dislocation

British Journal of Anaesthesia 111 (5): 800–6 (2013)
Advance Access publication 7 June 2013 · doi:10.1093/bja/aet198

BJA

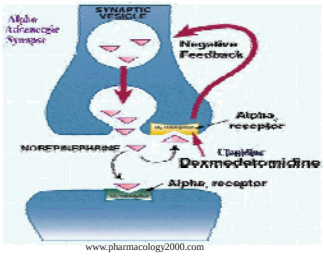
REGIONAL ANAESTHESIA

Dislocation rates of perineural catheters: a volunteer study

D. Marhofer[1,2], P. Marhofer[3]*, L. Triffterer[2], M. Leonhardt[4], M. Weber[1] and M. Zeitlinger[1]

[1] Department of Clinical Pharmacology, Medical University of Vienna, Vienna, Austria
[2] Department of Anaesthesiology and General Intensive Care Medicine, Medical University of Vienna, Vienna, Austria
[3] Department of Anaesthesiology and General Intensive Care Medicine, Head of Paediatric Anaesthesia, Medical University of Vienna, Vienna, Austria
[4] Medical University of Vienna, Vienna, Austria
* Corresponding author: Department of Anaesthesia, Intensive Care Medicine and Pain Therapy, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria. E-mail: peter.marhofer@meduniwien.ac.at

Results. We observed an overall dislocation rate of 15% (5% for interscalene catheters, 25% for femoral nerve catheters) and a significant correlation between time and rate of dislocations (r=0.99, P=0.001). US visualization of the spread of fluid was possible in all cases.



www.pharmacology2000.com

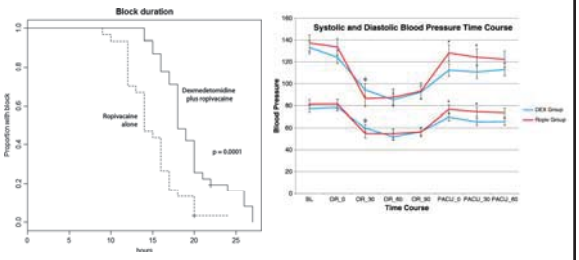
www.hospira.com

DEXMEDETOMIDINE AND REGIONAL ANESTHESIA

Dexmedetomidine Added to Ropivacaine Extends the Duration of Interscalene Brachial Plexus Blocks for Elective Shoulder Surgery When Compared with Ropivacaine Alone

A Single-Center, Prospective, Triple-Blind, Randomized Controlled Trial

Reg Anesth Pain Med 2014;39: 37–47



British Journal of Anaesthesia 110 (3): 438–42 (2013)
Advance Access publication 15 November 2012 · doi:10.1093/bja/aes400

BJA

Dexmedetomidine as an adjuvant to ropivacaine prolongs peripheral nerve block: a volunteer study

D. Marhofer[1], S. C. Kettner[1]*, P. Marhofer[1], S. Pils[2], M. Weber[2] and M. Zeitlinger[2]

[1] Department of Anaesthesia, Intensive Care Medicine and Pain Therapy and [2] Department of Clinical Pharmacology, Medical University of Vienna, Waehringer Guertel 18-20, A-1090 Vienna, Austria

* Corresponding author. E-mail: stephan.kettner@meduniwien.ac.at

	R	RpD	RpS
Sensory onset time (min)	19 (14)	13 (18)	16 (18)
Duration of sensory block (min)	350 (54)	555 (118)[1,2]	395 (40)[3]
Time until pinprick testing 100%	455 (70)	743 (152)[4,5]	518 (59)[6]
Motor onset time (min)	47 (36)	21 (15)[7]	43 (25)
Duration of motor block (min)	348 (74)	590 (92)[8,9]	438 (54)[10]

British Journal of Anaesthesia 110 (6): 915–25 (2013)
Advance Access publication 15 April 2013 · doi:10.1093/bja/aet066

BJA

Facilitatory effects of perineural dexmedetomidine on neuraxial and peripheral nerve block: a systematic review and meta-analysis

F. W. Abdallah[1] and R. Brull[2]*

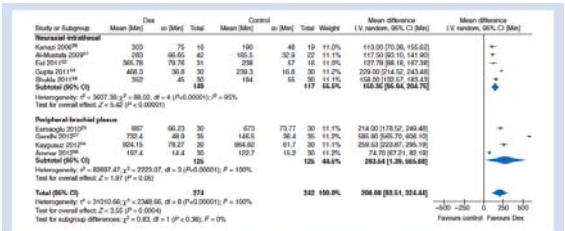


Fig 2 Forest plot showing sensory block duration. The sample size, mean, standard deviations, and the pooled estimates of the mean difference are shown. The 95% CIs are shown as lines for individual studies and as diamonds for pooled estimates.

Liposomal Bupivacaine

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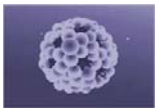
Liposomal Bupivacaine (Exparel®)



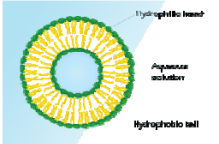
- DepoFoam®
  - Multivesicular spherical lipid particles in a honeycomb formation
  - Aqueous center containing encapsulated drug
  - Same delivery system as DepoDur®
- Approved only for surgical site infiltration
  - Contraindicated for paracervical blocks
  - Phase 2 and 3 trials for peripheral nerve blocks

Table 2: Comparison of Lipospheres and Liposomes

	Lipospheres	Liposomes
Components	Soybean oil, Lipid, Water	Phospholipid, Water
Lipid membrane	Monolayer single membrane	Mono- or multi-layer double membrane
Emulsion form	O/W	W/O/W
Incorporable drugs	Compounds soluble in soybean oil and retainable in lipids.	Water soluble compounds and compounds retainable in lipids.
Particle diameter	200 – 300 nm	Various sizes
Safety in vivo	Safe Clinically used as intravenous nutrition in 100 ml doses	Liposomes made of some lipids are toxic.
Stability	Stable for 24 months at room temperature. Lipo preparation are stored at 4°C	Rather unstable
Large-scale production	Suitable for mass production but a high pressure apparatus is necessary.	A special apparatus is not necessary at the research level. An apparatus for mass production has recently been developed.

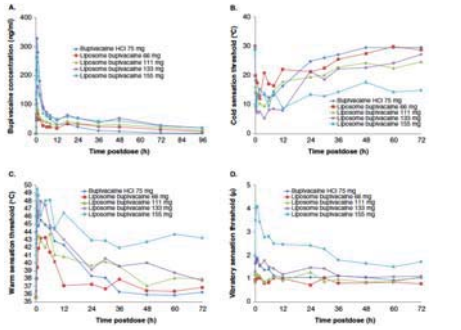
Int J Pharm Pharm Sci, Vol 3, Suppl 4, 17-21

http://www.google.co.in

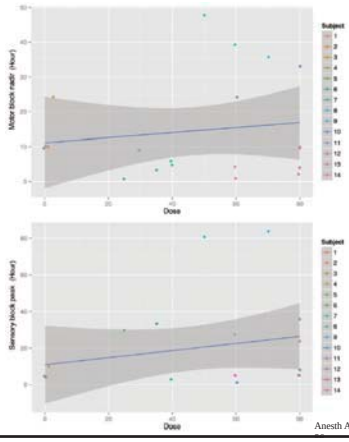


http://en.wikipedia.org/wiki/Liposome

Liposomal Bupivacaine: Femoral Block

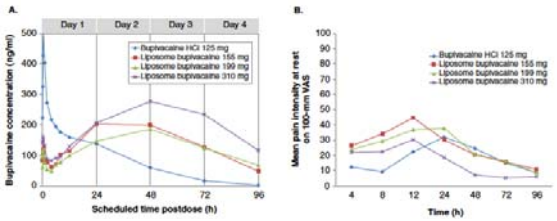


Expert Opin. Pharmacother. (2013) **14**(17)



Anesth Analg 2013;117:1248–

Liposomal Bupivacaine: Ankle Block



Expert Opin. Pharmacother. (2013) **14**(17)

Epidural Liposomal Bupivacaine: Motor Blockade

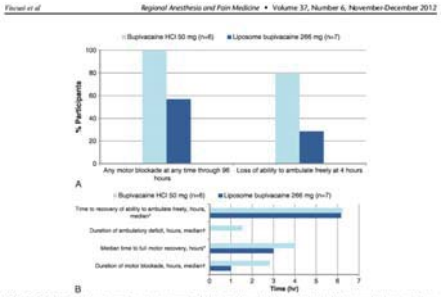


FIGURE 2. A, Proportion of participants experiencing motor blockade and loss of ability to ambulate in the liposome bupivacaine 266-mg and bupivacaine HCl groups. B, Duration of motor/ambulatory deficit and time to recovery in the liposome bupivacaine 266-mg and bupivacaine HCl groups. *Includes only subjects who experienced motor blockade or lost their ability to ambulate freely; †includes all subjects, whether or not they experienced motor blockade or lost their ability to ambulate freely.

Epidural Liposomal Bupivacaine: Sensory Blockade

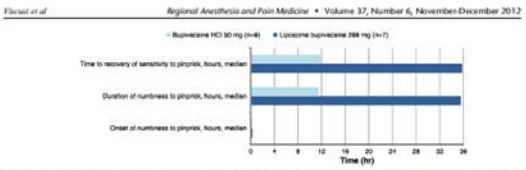


FIGURE 3. A, Summary of pinprick sensitivity assessments for the liposome bupivacaine 266-mg group and bupivacaine HCl group. B, Summary of cold sensitivity assessments for the liposome bupivacaine 266-mg group and bupivacaine HCl group.

Liposomal Bupivacaine Systemic Toxicity

Toxicity of Bupivacaine Encapsulated into Liposomes and Injected Intravenously: Comparison with Plain Solutions

Jean Boogaerts, MD, Anne Declercq, CRNA, Noelle Lafont, MD, Hassan Benameur, Eng, El Mustafa Akodad, Eng, Jean-Claude Dupont, MD*, and Franz J. Legros, PhD

Laboratory of Physiopathology, Free University of Brussels, Campus Erasme, Brussels, Belgium, and *Cardiac Department, Clinique Reine Fabiola, Montignies-sur-Sambre, Belgium

The acute central nervous system and cardiac toxicities of 0.25% bupivacaine, without adrenalin, encapsulated in multilamellar liposomes were compared with 0.25% plain solutions with and without adrenalin after intravenous infusion at a rate of 0.15 mg·kg^{-1}·min^{-1} with an increase of 0.035 mg·kg^{-1}·min^{-1} every 10 min. Three groups of six anesthetized, unventilated rabbits were studied. The doses of bupivacaine (in mg·kg^{-1}) which produced seizure, ventricular tachycardia, and asystole were determined. The doses of bupivacaine inducing seizure and ventricular tachycardia were significantly higher for liposomal bupivacaine than for the two plain solutions. A statistical comparison of the cumulative lethal doses of bupivacaine 0.25% with adrenalin and of liposomal bupivacaine led to a $P = 0.06$. Adrenalin did not modify the systemic toxicity of the local anesthetic. This study showed a reduction of nervous and cardiac toxicity of bupivacaine encapsulated in multilamellar liposomes when infused intravascularly.

(Anesth Analg 1993;76:553–5)

- Slow infusion of liposomal bupivacaine titrated to toxicity required larger doses
- No bolus, no temporal evaluation, no attempts at resuscitation
- Not using proprietary DepoFoam®

Liposomal Bupivacaine Local Toxicity

Research Article

The Safety of EXPAREL ® (Bupivacaine Liposome Injectable Suspension) Administered by Peripheral Nerve Block in Rabbits and Dogs *Journal of drug delivery (2090-3014)*, 2012 (12), p. 962101

In conclusion, a single administration of EXPAREL was demonstrated to be safe by peripheral nerve block in rabbits and dogs when tested in comparison with bupivacaine HCl and saline. EXPAREL did not cause overt irritation or local tissue damage even when injected at high dose or concentration around the brachial plexus nerve bundle.

Bupivacaine did not impact directly on neural tissue, and the findings of granulomatous inflammation were more consistent with a nonspecific foreign—body type reaction most likely mediated by the DepoFoam particles.

Liposomal Bupivacaine Compatibility

A review of the compatibility of liposome bupivacaine with other drug products and commonly used implant materials.
(PMID:24393760)

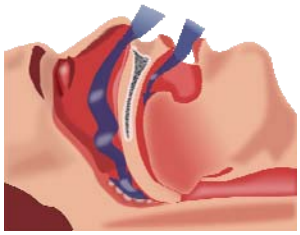
Postgrad Med. 2014 Jan;126(1):129-38

Liposome bupivacaine had **clinically meaningful interactions with other local anesthetics**, including lidocaine, ropivacaine, mepivacaine, or bupivacaine HCl (at liposome bupivacaine to bupivacaine HCl ratios < 2:1), which resulted in substantial displacement and release of free bupivacaine from liposomes . . .

Liposome bupivacaine may be locally administered after ≥ 20 minutes following local administration of lidocaine, ropivacaine, or mepivacaine.

The administration of **EXPAREL may follow the administration of lidocaine after a delay of 20 minutes or more**. Other formulations of bupivacaine should not be administered **within 96 hours** following administration of EXPAREL

www.exparel.com



www.nl.wikipedia.org

OBSTRUCTIVE SLEEP APNEA

OSA and Neuraxial Anesthesia

Sleep Apnea and Total Joint Arthroplasty under Various Types of Anesthesia

A Population-Based Study of Perioperative Outcomes

Stavros G. Memtsoudis, MD, PhD, FCCP, Ottokar Stundner, MD,* Rehana Rasul, MPH,† Xuming Sun, MS,† Ya-Lin Chiu, MS,† Peter Fleischut, MD,‡ Thomas Danninger, MD,* and Madhu Mazumdar, PhD†*

- 40, 316 database entries (>400 hospitals)
  - – Only 74% recorded type of anesthetic
- 75% total knee arthroplasty
- 11% neuraxial, 74% general, 15% combined
  - – 8% of general and 1% neuraxial had PNB

Reg Anesth Pain Med 2013;38: 274-281

OSA and Neuraxial Anesthesia

Sleep Apnea and Total Joint Arthroplasty under Various Types of Anesthesia

A Population-Based Study of Perioperative Outcomes

Stavros G. Memtsoudis, MD, PhD, FCCP, Ottokar Stundner, MD,* Rehana Rasul, MPH,† Xuming Sun, MS,† Ya-Lin Chiu, MS,† Peter Fleischut, MD,‡ Thomas Danninger, MD,* and Madhu Mazumdar, PhD†*

TABLE 3. Results From the Multivariate Regression for Various Outcomes

Multivariate Regression

	Neuraxial vs General		Combined Neuraxial/General vs General		Combined Neuraxial/General vs Neuraxial		
Outcome	**OR (95% CI)**	***P****	**OR (95% CI)**	***P****	**OR (95% CI)**	***P****	**C-Statistic**
Combined complications	0.825 (0.74–0.93)	0.0012	0.898 (0.82–0.99)	0.03	1.088 (0.95–1.25)	0.2399	0.64
Pulmonary complications	0.825 (0.65–1.05)	0.1154	0.772 (0.63–0.95)	0.0137	0.935 (0.70–1.26)	0.659	0.63
Cardiac complications	0.904 (0.78–1.05)	0.1859	0.936 (0.83–1.06)	0.3121	1.035 (0.86–1.24)	0.7069	0.70
Blood transfusion	0.919 (0.81–1.04)	0.1776	0.87 (0.78–0.97)	0.0116	0.947 (0.81–1.10)	0.4821	0.64
Mechanical ventilation	0.636 (0.50–0.80)	0.0001	0.644 (0.53–0.79)	<0.0001	1.012 (0.76–1.35)	0.9334	0.59
Critical care service admission	0.433 (0.34–0.55)	<0.0001	0.666 (0.56–0.79)	<0.0001	1.538 (1.16–2.03)	0.0025	0.61
Prolonged length of stay	0.752 (0.69–0.82)	<0.0001	0.70 (0.65–0.76)	<0.0001	0.93 (0.83–1.04)	0.202	0.60
Increased cost of hospitalization	0.883 (0.80–0.98)	0.0139	0.704 (0.64–0.77)	<0.0001	0.797 (0.70–0.90)	0.0004	0.57

Reg Anesth Pain Med 2013;38: 274-281

Obesity and Interscalene PNB

Review Article

Review of interscalene block for postoperative analgesia after shoulder surgery in obese patients

Bassam Al-Nasser*

Department of Anesthesia and Intensive Care, Clinique du Parc Saint Lazare, Beauvais, France

"There are **neither evidence-based data nor studies on the use of ISB for postoperative analgesia after shoulder surgery in the obese population**. However, the overall consensus supports the concept of multimodal analgesia and the **preferential use of regional anesthetic technique**"

Therefore, in order to reduce phrenic nerve involvement after ISB, the following essential points are suggested:
(1) Ultrasound guidance;
(2) A **low volume** of local anesthetic on initial injection and low-volume continuous perfusion;
(3) Injection through the catheter;
(4) Needle and catheter placement at the **C7 root**.

Acta Anaesthesiologica Taiwanica 2012;50:29-34

Society for Ambulatory Anesthesia Consensus Statement on Preoperative Selection of Adult Patients with Obstructive Sleep Apnea Scheduled for Ambulatory Surgery

Girish P. Joshi, MBBS, MD, FFARSCI,* Saravanan P. Ankichetty, MD, DA, MBA,†
Tong J. Gan, MD, MHS, FRCA,† and Frances Chung, MBBS, FRCPC†

S = Snoring. Do you snore loudly (louder than talking or loud enough to be heard through closed doors)?
T = Tiredness. Do you often feel tired, fatigued, or sleepy during daytime?
O = Observed apnea. Has anyone observed you stop breathing during your sleep?
P = Pressure. Do you have or are you being treated for high blood pressure?
B = BMI > 35 kg/m²
A = Age > 50 years
N = Neck circumference > 40 cm
G = Male gender

From Hathaway, 2006.[15] Fewer than 3 questions positive = low risk of OSA; 3 or more questions positive: high risk of OSA; 5 to 8 questions positive: high probability of moderate-to-severe OSA.[11]

Anesth Analg 2012;115:1060–8

Society for Ambulatory Anesthesia Consensus Statement on Preoperative Selection of Adult Patients with Obstructive Sleep Apnea Scheduled for Ambulatory Surgery

Girish P. Joshi, MBBS, MD, FFARSCI,* Saravanan P. Ankichetty, MD, DA, MBA,†
Tong J. Gan, MD, MHS, FRCA,† and Frances Chung, MBBS, FRCPC†

"painful ambulatory surgery may not be suitable if postoperative pain relief cannot be predominantly provided with nonopioid analgesic techniques. **Local/regional analgesia**, acetaminophen, and nonsteroidal anti-inflammatory drugs or cyclooxygenase-2 specific inhibitors **should be used as primary analgesic techniques**"

"the potential risks can last for several days after surgery"

Anesth Analg 2012;115:1060–8

Perioperative Management of Obstructive Sleep Apnea

Adebola O. Adesanya, MD, FCCP; Won Lee, MD; Nancy B. Greilich, MD; and Girish P. Joshi, MD

"Surgical stress and pain have been shown to independently influence sleep patterns manifesting as postoperative sleep deprivation, sleep fragmentation, and reduction in rapid eye movement sleep. The subsequent **rebound in rapid eye movement sleep** is accompanied by **increased vulnerability to airway obstruction and apnea that can last for several days**. This sleep disturbance appears to be related to the location and invasiveness of the surgical procedure?

"Patients who undergo surgery under regional anesthesia should have the **regional anesthetic continued into the PAR and beyond if possible**. Other patients should be evaluated for placement of regional analgesia for postoperative pain control"

"Patients who undergo surgery under a regional anesthetic block are also required to be monitored for **additional 3 [hours] in the PAR** even when supplemental sedatives have not been used"

Chest 2010; 138(6): 1489 – 1498

Practice Guidelines for the Perioperative Management of Patients with Obstructive Sleep Apnea

An Updated Report by the American Society of Anesthesiologists Task Force on Perioperative Management of Patients with Obstructive Sleep Apnea

Anesthesiology 2014; 120:268-86

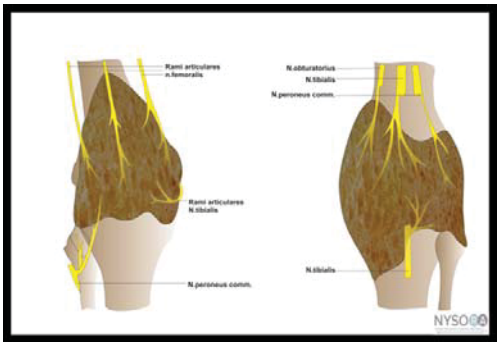
"The literature is insufficient to evaluate outcomes associated with postoperative peripheral regional versus systemic analgesic techniques on patients with OSA"

		Percent Responding to Each Item				
	N	Strongly Agree	Agree	Equivocal	Disagree	Strongly Disagree
V. Postoperative management						
20. Regional analgesic techniques should be considered to reduce or eliminate the requirement for systemic opioids in patients at increased perioperative risk from OSA	267	56.6*	38.6	4.9	0.0	0.0
13. For superficial procedures, consider the use of local anesthesia or peripheral nerve blocks, with or without moderate sedation	267	58.4*	34.8	6.0	0.4	0.4

www.bbc.co.uk

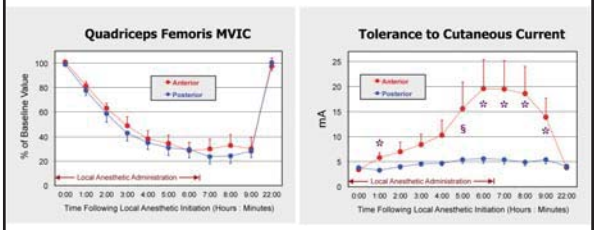
TOTAL KNEE ARTHROPLASTY

Innervation – Knee Joint



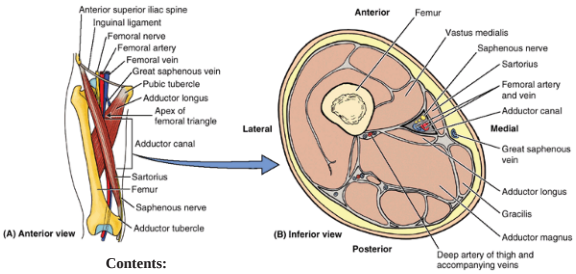
Continuous Femoral Nerve Blocks: The Impact of Catheter Tip Location Relative to the Femoral Nerve (Anterior Versus Posterior) on Quadriceps Weakness and Cutaneous Sensory Block

Brian M. Ilfeld, MD, MS,* Vanessa J. Loland, MD,* NavParkash S. Sandhu, MD,* Preetham J. Suresh, MD,* Michael J. Bishop, MD,* Michael C. Donohue, PhD,† Eliza J. Ferguson, BS,* and Sarah J. Madison, MD*



Anesth Analg 2012;115:721–7

Adductor Canal



Contents:

1. **Femoral Artery and Vein**
2. **Saphenous Nerve**
3. **Nerve to Vastus Medialis**
4. **Posterior Branch of Obturator Nerve**

http://dermatologic.com.ar

Adductor Canal Block *versus* Femoral Nerve Block for Total Knee Arthroplasty

A Prospective, Randomized, Controlled Trial

David H. Kim, M.D., Yi Lin, M.D., Ph.D., Enrique A. Goytizolo, M.D., Richard L. Kahn, M.D., Daniel B. Maalouf, M.D., M.P.H., Asha Manohar, M.D., Minda L. Patt, M.D., Amanda K. Goon, B.A., Yuo-yu Lee, M.S., Yan Ma, Ph.D., Jacques T. YaDeau, M.D., Ph.D.

Anesthesiology 2014; 120:epub

Adductor Canal Block Versus Femoral Nerve Block for Analgesia After Total Knee Arthroplasty

A Randomized, Double-blind Study

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Reg Anesth Pain Med 2013;38: 526–532

The Effects of Ultrasound-Guided Adductor Canal Block Versus Femoral Nerve Block on Quadriceps Strength and Fall Risk

A Blinded, Randomized Trial of Volunteers

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Reg Anesth Pain Med 2013;38: 321–325

Adductor Canal Block *versus* Femoral Nerve Block and Quadriceps Strength

A Randomized, Double-blind, Placebo-controlled, Crossover Study in Healthy Volunteers

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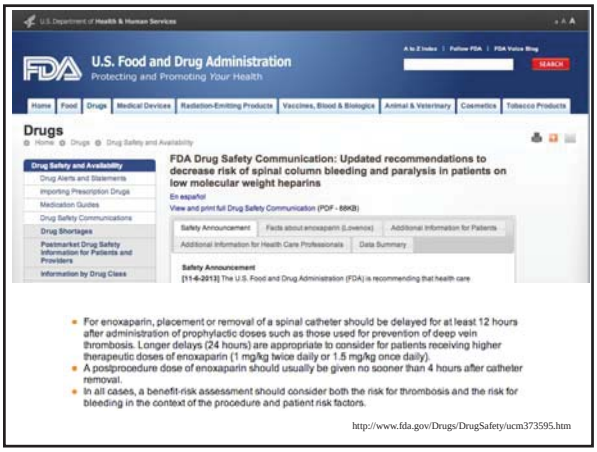
Anesthesiology 2013;118:409-15



http://www.fda.gov/Drugs/DrugSafety/ucm373595.htm

Spinal Epidural Hematoma After Spinal Cord Stimulator Trial Lead Placement in a Patient Taking Aspirin

Reg Anesth Pain Med 2014;39: 70–72

Epidural Hematomas After Removal of Percutaneous Spinal Cord Stimulator Trial Leads
Two Case Reports

Reg Anesth Pain Med 2014;39: 73–77

Interventional Pain Techniques

Assessment of Bleeding Risk of Interventional Techniques: A Best Evidence Synthesis of Practice Patterns and Perioperative Management of Anticoagulant and Antithrombotic Therapy

Recommendations: The recommendations derived from the comprehensive assessment of the literature and guidelines are to continue NSAIDs and low dose aspirin, and phosphodiesterase inhibitors (dipyridamole, cilostazol, Aggrenox) during interventional techniques. However, the recommendations for discontinuation of antiplatelet therapy with platelet aggregation inhibitors (clopidogrel, ticlopidine, prasugrel) is variable with clinical judgment to continue or discontinue based on the patient's condition, the planned procedure, risk factors, and desires, and the cardiologist's opinion. Low molecular weight heparin (LMWH) or unfractionated heparin may be discontinued 12 hours prior to performing interventional techniques. Warfarin should be discontinued or international normalized ratio (INR) be normalized to 1.4 or less for high risk procedures and 2 or less for low risk procedures based on risk factors. It is also recommended to discontinue Pradaxa for 24 hours for paravertebral interventional techniques in 2 to 4 days for epidural interventions in patients with normal renal function and for longer periods of time in patients with renal impairment, and to discontinue rivaroxaban for 24 hours prior to performing interventional techniques.

Pain Physician 2013; 16:-SE261-SE318

British Journal of Anaesthesia 111 (S1): i96–i113 (2013)
doi:10.1093/bja/aet401

BJA

REGIONAL ANAESTHESIA

New oral anticoagulants and regional anaesthesia

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Drug	Time to peak effect of drug	Resumption of drug based on 8 h minus the time to peak anticoagulant effect*	Resumption of drug based on 24 h minus the time to peak anticoagulant effect†	Baron and colleagues:[12] recommendations (high-risk procedures)	Connolly and Spyropoulos:[13] high bleeding risk	Liew and Douketis:[14]
Dabigatran	2 (1.5–3) h	6 h	22 h	48 h	24 h, half of the usual dose for first 2 days	24 h after operation for cases with low bleeding risk, 48–72 h for high bleeding risk
Rivaroxaban	2.5–4 h	5.5 h	21.5 h	48 h	24 h, half of the usual dose for first 2 days	Same as dabigatran
Apixaban	1–2 h	7 h	23 h	48 h	24 h, half of the usual dose for first 2 days	Same as dabigatran
Prasugrel	1 h	7 h	23 h	Caution (recommended within 24 h for aspirin and clopidogrel)		
Ticagrelor	2–4 h	6 h	22 h	(Same as for prasugrel)		

Anticoagulants – Half Lives

Drug	Metabolism, renal, and faecal/biliary elimination*	Elimination half-life	Five half-lives	Baron and colleagues:[12] recommendations	Connolly and Spyropoulos:[13] high bleeding risk (4–5 half-lives between dose and surgery)	Liew and Douketis:[14] no or minimal anticoagulant effect at surgery (four to five half-lives)
Dabigatran	Renal 80%, faecal 20%	12–17 h 28 h (end-stage renal disease)	85 h (4 days) 140 (6 days) (end-stage renal disease)	1–2 days with CrCl ≥ 50 ml min^{-1}; 3–5 days with CrCl < 50 ml min^{-1}	3 days with CrCl > 50 ml min^{-1}; 4–5 days with CrCl 30–50 ml min^{-1}	3 days with CrCl > 50 ml min^{-1}; 4–5 days with CrCl 30–50 ml min^{-1}
Rivaroxaban	Metabolism 33%, renal 33% (33% inactive metabolites)	9–13 h	65 h (3 days)	≥1 day with normal renal function; 2 days with CrCl 60–90 ml min^{-1}; 3 days with CrCl 30–59 ml min^{-1}; 4 days with CrCl 15–29 ml min^{-1}	3 days with CrCl > 50 ml min^{-1} and CrCl 30–50 ml min^{-1}; 4 days with CrCl 15–29.9 ml min^{-1}	3 days with CrCl > 50 ml min^{-1}; 4–5 days with CrCl 30–50 ml min^{-1}
Apixaban	Renal 25%, metabolism and faecal elimination 75%	15.2 (8.5)	75 h (3–4 days)	1 or 2 days with CrCl > 60 ml min^{-1}; 3 days with CrCl 50–59 ml min^{-1}; 5 days with CrCl < 30–49 ml min^{-1}	3 days with CrCl > 50 ml min^{-1}; 4 days with CrCl 30–50 ml min^{-1}	(Same as rivaroxaban)

Anticoagulants – Lab Monitoring

Table 5 Utility of coagulation assays and reversal of new anticoagulants. *There is no specific antidote for dabigatran, rivaroxaban, and apixaban. PCC, prothrombin complex concentrate; PT, prothrombin time; PTT, partial thromboplastin time; TEG, thrombelastography; TT, thrombin time. The authors have no experience with multiple electrode platelet aggregometry (Multiplate)

	Dabigatran	Rivaroxaban	Apixaban	Prasugrel	Ticagrelor
Recommended coagulation assay	Dilute TT, also called TCT—sensitive aPTT—sensitive (relationship not linear) and readily available ECT—sensitive but not readily available Anti-factor II assay	PT Anti-Xa assay	Anti-Xa assay Dilute PT	$P2Y_{12}$ assay Platelet mapping portion of the TEG Multiple electrode platelet aggregometry (Multiplate)	$P2Y_{12}$ assay Platelet mapping portion of the TEG Multiple electrode platelet aggregometry (Multiplate)
Reversal*	Dialysis Activated charcoal (within 1–2 h of ingestion) Dabigatran-neutralizing antibody in development	Activated charcoal (within 8 h of ingestion) Four-factor PCC	Activated charcoal (within 3 h of ingestion)	Platelets	Platelets

Antithrombotic or Thrombolytic Medication	Time from last medication dose to neuraxial block (hours)	Time from neuraxial block to subsequent medication dose (hours)	Time from last medication dose to catheter removal (hours)	Time from catheter removal to subsequent medication dose (hours)	Pharmacologic reversibility	Lab monitor
Unfractionated heparin (IV)	> 4 and normal aPTT	1	> 4 and normal aPTT	1	Protamine	aPTT
Unfractionated heparin (SQ)	Suggest block first, Possible risk at 1-2 hour	Immediate	Immediate	Immediate	Protamine	No
Low-molecular weight heparin (daily prophylaxis)	10-12	6-8	10-12	4	No	No
Low-molecular weight heparin (twice daily prophylaxis)	24	NOT RECOMMENDED	NOT RECOMMENDED	4	No	No
Warfarin	CHRONIC: 4-5 days and normal INR INITIATING: <24 hours	Immediate	INR < 1.5 or INR < 3 and monitored until stabilized	Immediate	Vitamin K, plasma, Octaplex	INR
Aspirin (low dose) (high dose)	Immediate 7 days?	Immediate	Immediate	Immediate	No	No
NSAIDS + heparin/warfarin	NO DATA	NOT RECOMMENDED	NOT RECOMMENDED	NO DATA	No	No
Thienopyridines	CLOPIDOGREL: 7 days or 5 with normal platelet fxn TICLOPIDINE: 14 days PRASUGREL: likely 7 days	NOT RECOMMENDED	NOT RECOMMENDED	NO DATA	No	PFA II
Glycoprotein IIb/IIa Receptor Antagonists	EPTIFIBATIDE: 8 TIROFIBAN: 8 ABCIXIMAB: 24-48	NOT RECOMMENDED	NOT RECOMMENDED	NO DATA	No	No
Fibrinolytics / Thrombolytics	NO DATA	10 days	NOT RECOMMENDED	NO DATA	No	Fibrinogen ?
Fondaparinux	NO DATA	NOT RECOMMENDED	NOT RECOMMENDED	2	No	Xa
Direct Thrombin Inhibitors	NO DATA	NOT RECOMMENDED	NOT RECOMMENDED	NO DATA	No	aPTT
Dabigatran Etexilate	48-84 ?	NO DATA	NO DATA	NO DATA	No	aPTT (non-linear)
Rivaroxaban Herbals	24 ? Immediate	NO DATA Immediate	NO DATA Immediate	NO DATA Immediate	Factor VIIa	PT, PTT, Heptest No