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Update Management of Local Anesthesia Focus on Bupivacaine and Ropivacaine

What is Regional Anesthesia....??

- ❑ Regional anesthesia is a **method of pain prevention** for surgeries and procedures
- ❑ Only the area of the body that would feel pain is numbed → patient still **conscious**
- ❑ Injected near the spinal canal to block sensations in the lower body or limbs → **Spinal & Epidural**



Why Regional Anesthesia Is Used...??

- ❖ One benefit of a regional anesthetic is the patient can be consciously sedated or be fully conscious
- ❖ A C-section is an example of a procedure performed with the patient awake, with regional anesthesia (epidural) used to control the pain of the surgery
- ❖ The patient can feel things above the abdomen, and she is able to carry on a conversation and see her newborn immediately after birth
- ❖ By using regional anesthesia, the baby's exposure to sedating drugs is lessened.

Local Anesthetic Drug

Agent	Techniques	Concentrations Available	Maximum Dose (mg/kg)	Typical Duration of Nerve Blocks ¹
Esters				
Benzocaine	Topical ²	20%	NA ³	NA
Chloroprocaine	Epidural, infiltration, peripheral nerve block, spinal ⁴	1%, 2%, 3%	12	Short
Cocaine	Topical	4%, 10%	3	NA
Procaine	Spinal, local infiltration	1%, 2%, 10%	12	Short
Tetracaine (amethocaine)	Spinal, topical (eye)	0.2%, 0.3%, 0.5%, 1%, 2%	3	Long
Amides				
Bupivacaine	Epidural, spinal, infiltration, peripheral nerve block	0.25%, 0.5%, 0.75%	3	Long
Lidocaine (lignocaine)	Epidural, spinal, infiltration, peripheral nerve block, intravenous regional, topical	0.5%, 1%, 1.5%, 2%, 4%, 5%	4.5 7 (with epinephrine)	Medium
Mepivacaine	Epidural, infiltration, peripheral nerve block, spinal	1%, 1.5%, 2%, 3%	4.5 7 (with epinephrine)	Medium
Prilocaine	EMLA (topical), epidural, intravenous regional (outside North America)	0.5%, 2%, 3%, 4%	8	Medium
Ropivacaine	Epidural, spinal, infiltration, peripheral nerve block	0.2%, 0.5%, 0.75%, 1%	3	Long

¹Wide variation depending on concentration, location, technique, and whether combined with a vasoconstrictor (epinephrine). Generally, the shortest duration is with spinal anesthesia and the longest with peripheral nerve blocks.

²No longer recommended for topical anesthesia.

³NA, not applicable or not defined.

⁴Recent literature describes this agent for short-duration spinal anesthetics.

Marcaïn®

ORIGINAL



Marcaïn Injeksi 20 ml



Marcaïn Spinal Heavy 4 ml

“High Quality with Proven Efficacy and Safety Profile”

A Wide Variety of Therapeutic Indications of **Marcaine® 0.5% Spinal Heavy (Hyperbaric Bupivacaine)**

Marcaine® 0.5% Spinal Heavy is produced by the addition of dextrose (80 mg/mL) to isobaric bupivacaine¹.

Marcaine® 0.5% Spinal Heavy is indicated as intrathecal (subarachnoid and spinal) anesthesia for surgical and obstetrical procedures including¹:



Lower abdominal surgery
including Cesarean section



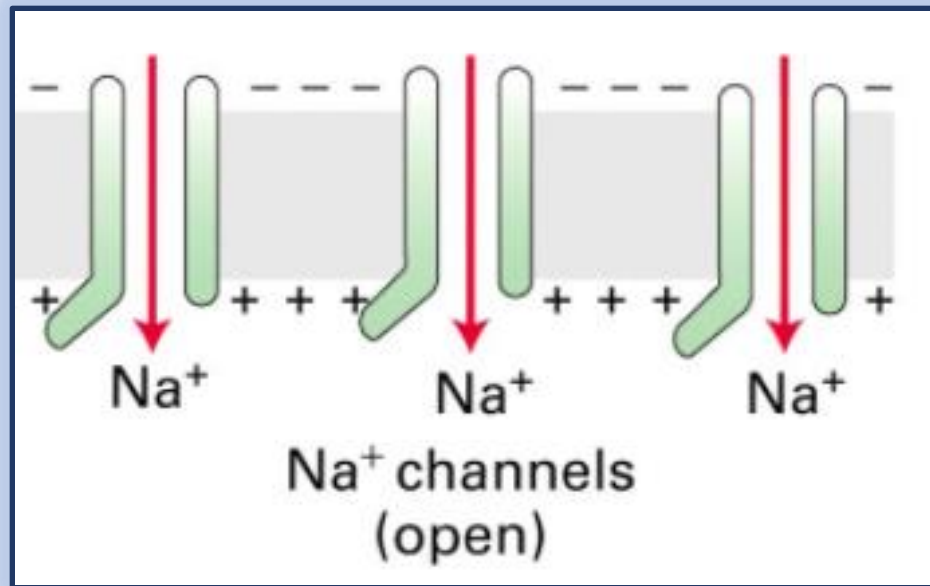
Urological surgery



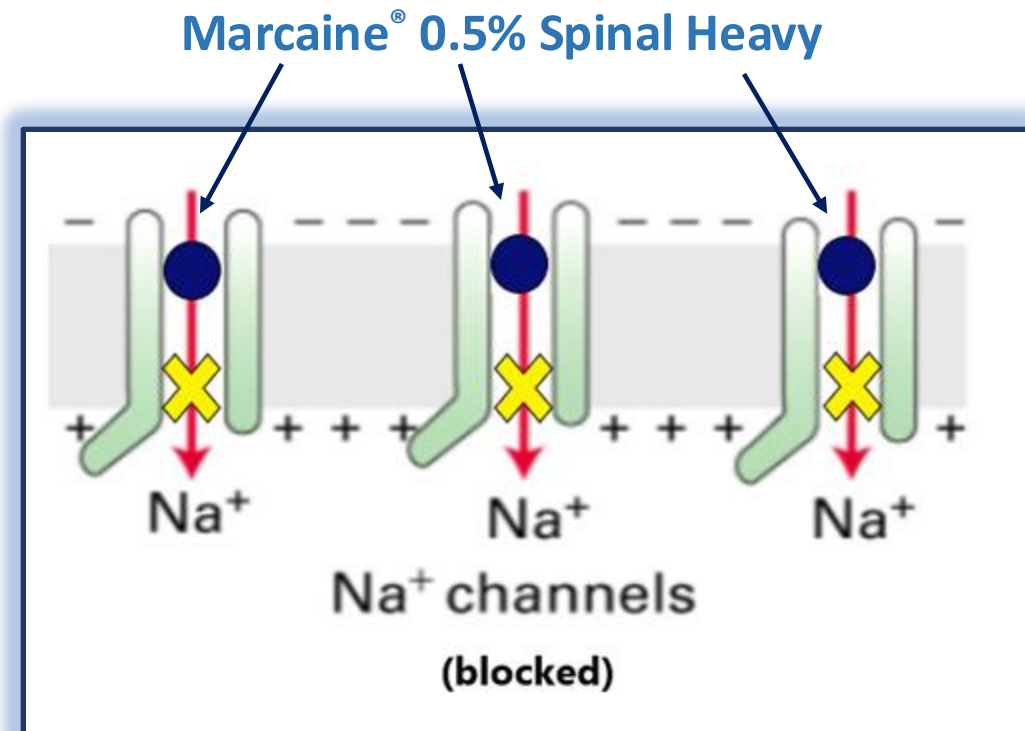
Lower limb surgery including
hip surgery lasting 1.5-3 hours

Mechanism of Action of Marcaine® 0.5% Spinal Heavy

Marcaine® 0.5% Spinal Heavy inhibits depolarization and nerve impulse conduction by reversibly binding to specific sodium ion channels in the neuronal membrane and preventing the influx of sodium ions through the nerve membrane^{1,2}.



Depolarization



Depolarization is inhibited

Dosage Recommendations of **Marcaine® 0.5% Spinal Heavy** in Adults

The dose should be reduced in the elderly and patients in the late stages of pregnancy¹.

Dosage recommendations in adults¹

Type of surgery	Concentration (mg/mL)	Volume (mL)	Dose (mg)	Onset (minute)	Duration (hour)
Urological surgery	5.0	1.5-3	7.5-15	5-8	2-3
Lower abdominal surgery (including Cesarean section) and lower limb surgery including hip surgery	5.0	2-4	10-20	5-8	1.5-3

Dosage Recommendations of Marcaine[®] 0.5% Spinal Heavy in Children

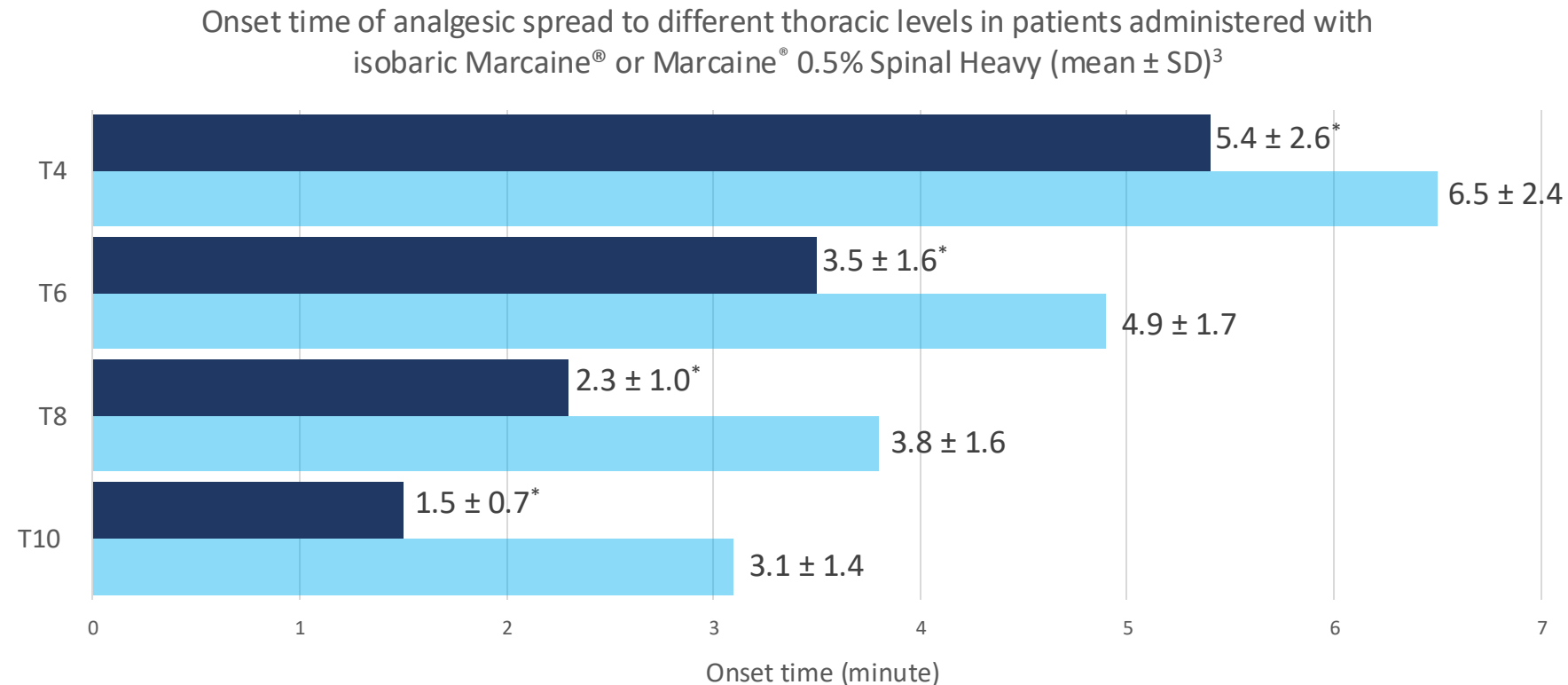
A relatively higher CSF volume is observed in infants and neonates which requires a relatively larger dose/kg of anesthesia to produce the same level of block as compared to adults¹.

Dosage recommendations in children¹

Body weight (kg)	Dose (mg/kg)
<5	0.40-0.50
5 to 15	0.30-0.40
15 to 40	0.25-0.30

Shorter Onset Time of **Marcaine® 0.5% Spinal Heavy** to Establish the Block versus Isobaric Marcaine®³

Marcaine® 0.5% Spinal Heavy required less time to establish the block compared with that of the isobaric Marcaine® in Cesarean section³.



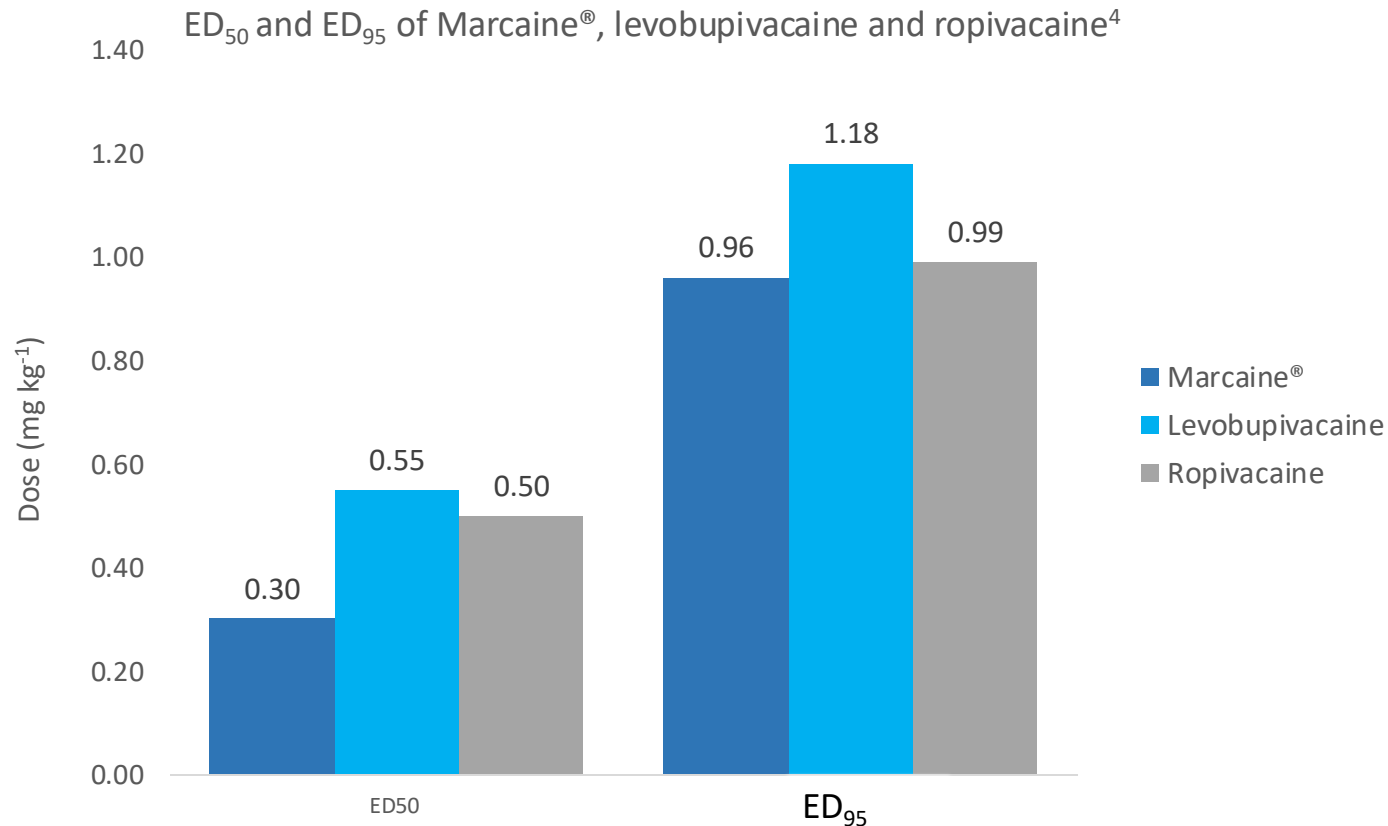
*p<0.01 versus isobaric bupivacaine.

■ Marcaine® 0.5% Spinal Heavy ■ Isobaric Marcaine®

Study design³: 98 patients were recruited in this randomized and double-blind study and randomly assigned to receive isobaric Marcaine® (n=48) or Marcaine® 0.5% Spinal Heavy (n=50) as spinal anesthesia in Cesarean section. The onset time of 2 anesthetic agents to establish block was measured and compared in this study.

Higher Potency of Marcaine® versus Levobupivacaine and Ropivacaine⁴

Marcaine® was more potent than levobupivacaine and ropivacaine with lower ED₅₀ and ED₉₅ doses estimated by isotonic regression in the study⁴.



*Increasing
potency*

Study design⁴:

The data of enrolled 148 infants were analyzed in this two-stage study. In this study, isobaric Marcaine®, ropivacaine and levobupivacaine were used as spinal anesthesia in infants. ED₅₀ and ED₉₅ doses of Marcaine®, levobupivacaine and ropivacaine were determined by the analysis of the combined phase 1 and 2 data sets in this study.

Favorable Antimicrobial Efficacy of **Marcaine®** against a Wider Range of Bacteria versus Levobupivacaine⁵

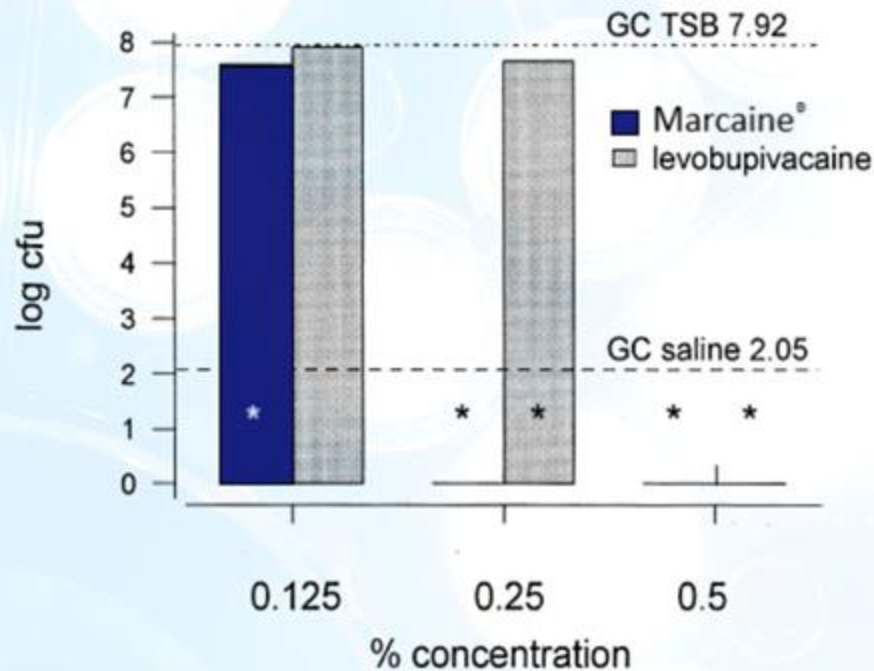
Inhibitory properties of Marcaine® and levobupivacaine for various bacteria⁵

Bacteria	Marcaine®	Levobupivacaine
<i>Candida albicans</i>	✓	-
<i>Escherichia coli</i>	✓	-
<i>Enterococcus faecalis</i>	✓	✓
MRSA	✓	-
<i>Pseudomonas aeruginosa</i>	✓	-
<i>Staphylococcus aureus</i>	✓	✓
<i>Staphylococcus epidermidis</i>	✓	✓
<i>Streptococcus pneumoniae</i>	✓	-
Other pathogens	<i>Bacillus</i> species, <i>Bacillus cereus</i> , <i>Candida</i> species, <i>Corynebacterium</i> species, MSSA, <i>Micrococcus</i> species, <i>Streptococcus pyogenes</i>	-

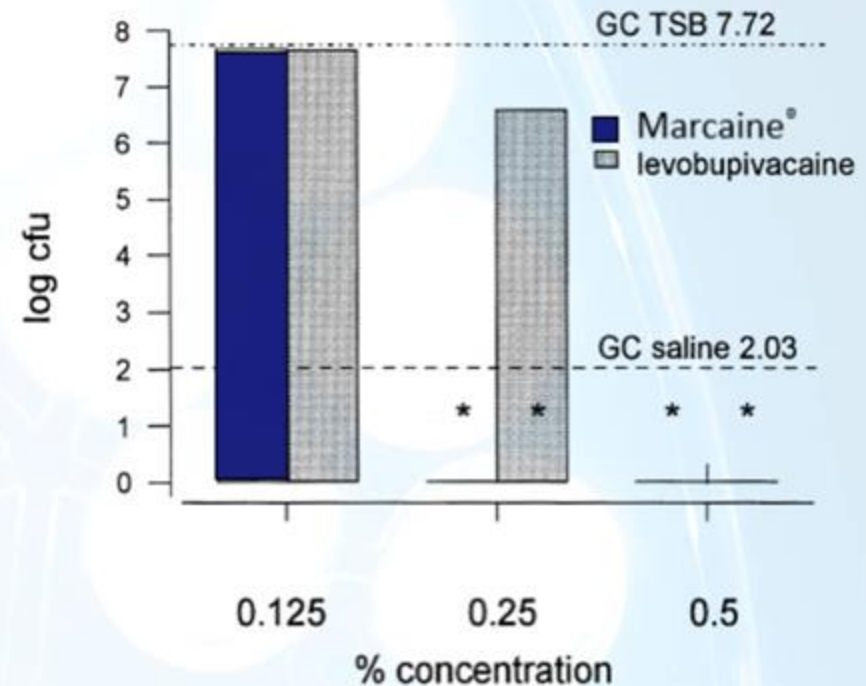
More Potent Antibacterial Action of Marcaine® against *S. aureus* and *S. epidermidis* versus Levobupivacaine⁶

The bacteria most commonly implicated in epidural catheter-associated infection are *S. aureus* and *S. epidermidis*, whereas a lower minimum bactericidal concentration of Marcaine® (0.25%) could be observed compared with that of levobupivacaine (0.5%)⁶.

Log of mean cfu per 100 µL of test solution (log cfu) of *S. aureus* against Marcaine® and levobupivacaine concentration⁶



Log of mean cfu per 100 µL of test solution (log cfu) of *S. epidermidis* against Marcaine® and levobupivacaine concentration⁶



Possible Contributing Factors of the Failure of Spinal Anesthesia¹⁰

Anatomic abnormalities of the spine

Inadequate intrathecal spread of the anesthetic

Patient's resistance to a specific anesthetic

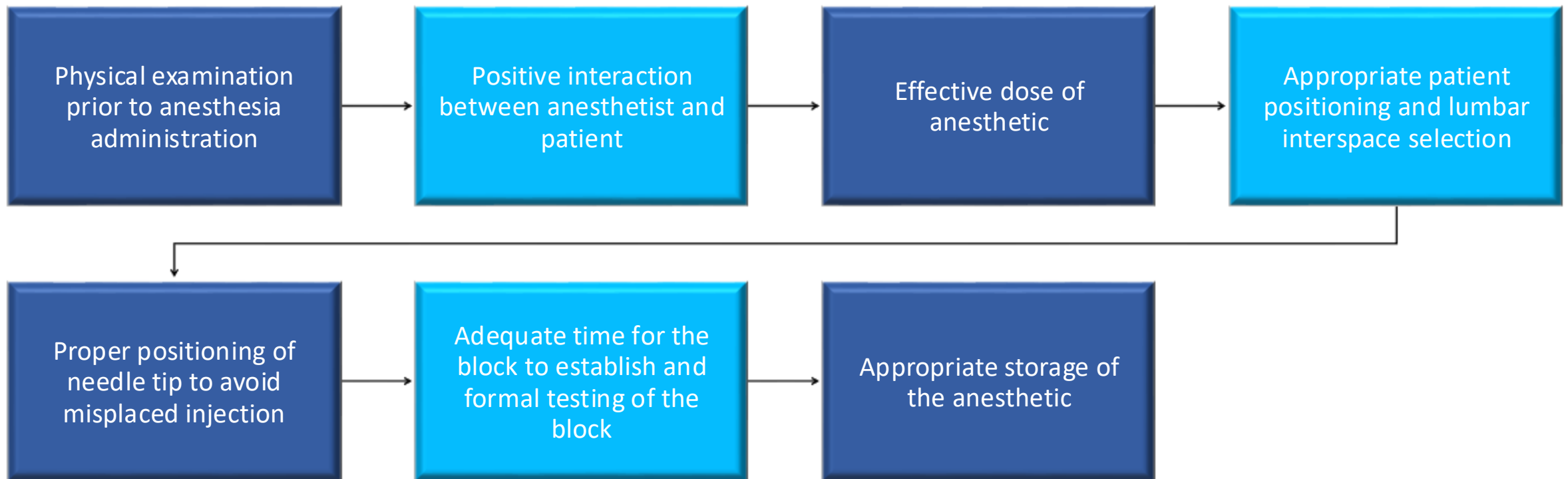
Lumbar interspace selection

Drug dosage

Failed lumbar puncture

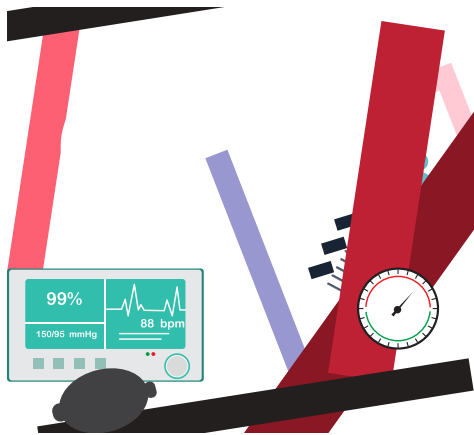
Patient positioning

Practical Reminders of Spinal Anesthesia Administration¹¹⁻¹³



Choose the Right Dose of Anesthetic

- Potential benefits of using lower dose of hyperbaric Marcaine[®] (5-10 mg rather than 15 mg)¹³



Minimize hypotension by
producing unilateral block



Speed postoperative mobilization
by decreasing duration

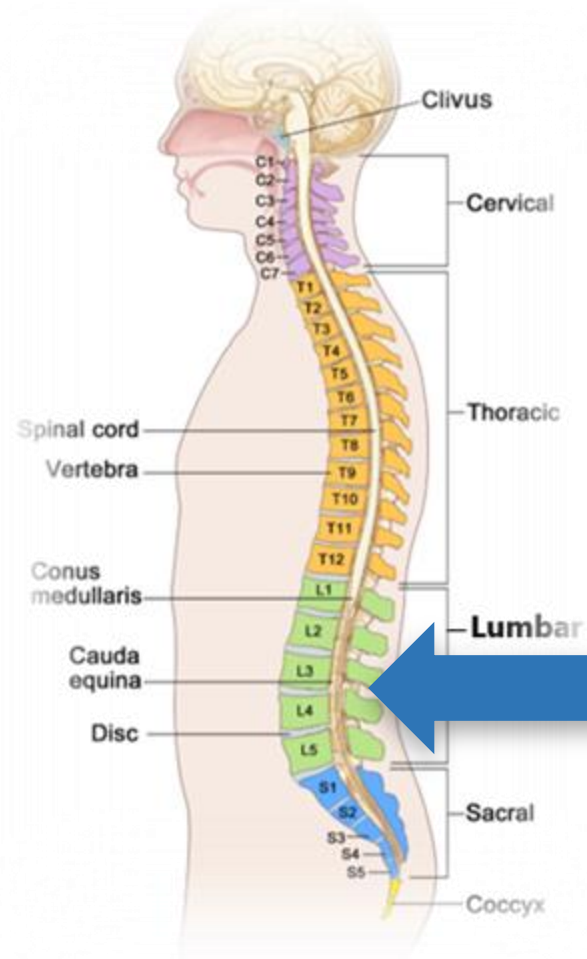
Position the Patients on a Firm Flat Surface with Maximal Flexion to Open the Lumbar Spine¹¹



To facilitate needle insertion between the spinal vertebrae:

- ✓ Flex the whole spine including the neck, the hips, and knees¹³
- ✓ Avoid rotation and lateral curvature of the spine¹³

Select A Proper Lumbar Interspace to Facilitate the Insertion of the Spinal Needle



Only perform spinal anesthesia in lumbar area, specifically the mid to low lumbar levels⁸

- Avoid damage to the spinal cord⁸
- Prevent intrathecally-injected medications from having any activity in the upper thoracic and cervical regions⁸

The recommended injection site of **Marcaine® 0.5% Spinal Heavy** is the L3-L4 intervertebral space¹

Check the Patency of Needle Prior to Insertion¹¹



- ✓ Do not use blocked needles¹¹
- ✓ Do not advance the needle without the stylet in place¹¹
- ✓ Discard the bent and crooked needle¹¹

Prevent Injectate Loss during Spinal Anesthesia Administration

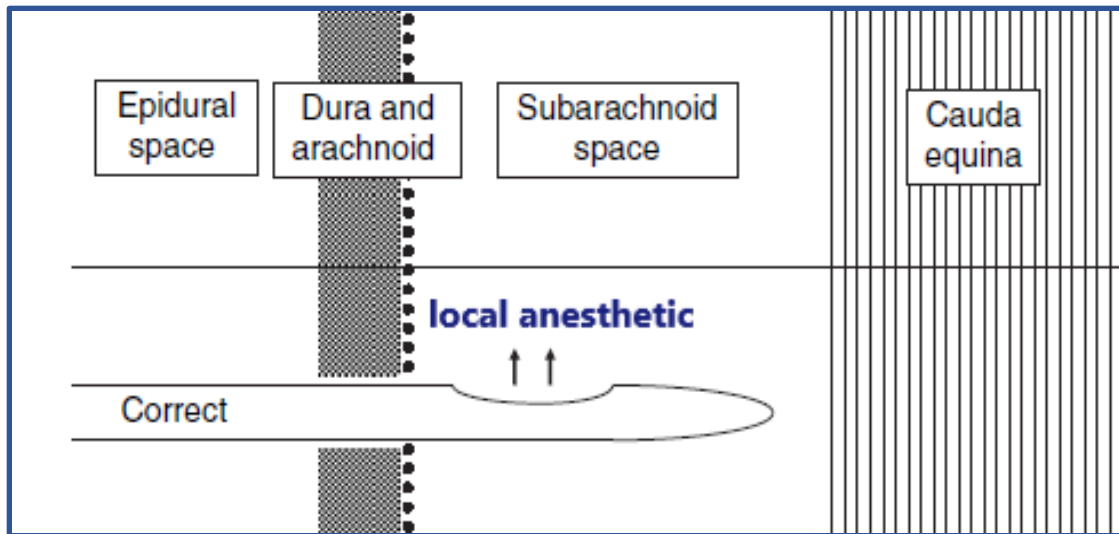


To prevent leakage of injected volume due to poor connection between the needle and the syringe¹¹:

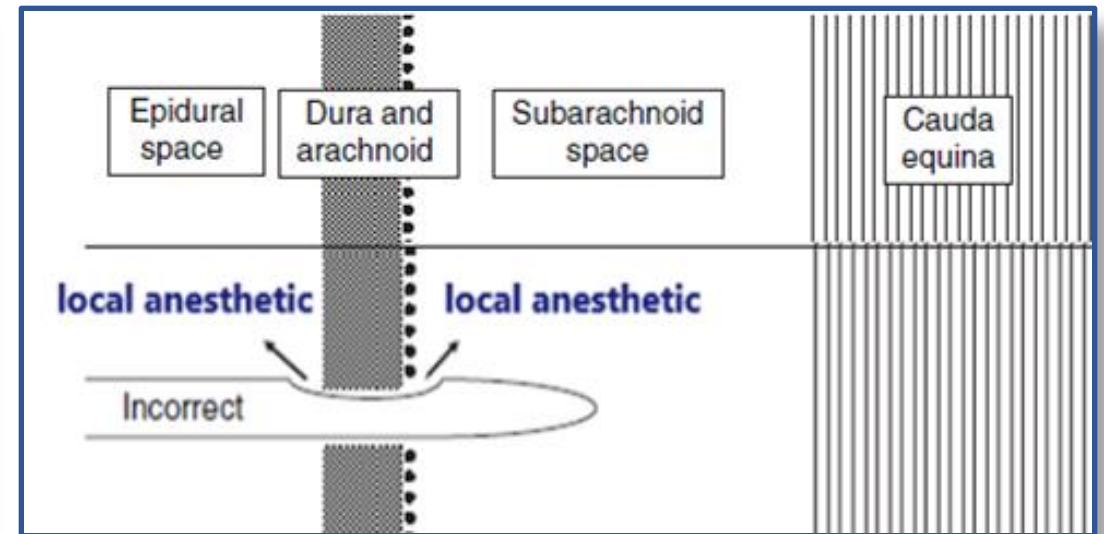
- ✓ Ensure that the needle tip does not get displaced¹¹
- ✓ Firmly secure the syringe during drug injection¹¹
- ✓ Confirm intrathecal delivery of the drug by checking CSF aspiration before injecting and before completion of injection of local anesthetics¹¹

Minimize the Possibility of Misplaced Injection of Anesthetic

Great care should be taken to avoid either anterior or posterior displacement of the needle tip from subarachnoid to epidural space, where deposition of a spinal dose of local anesthetic will have little or no effect¹³.



All local anesthetic solution can reach the subarachnoid space if the pencil-point needle is correctly placed¹³.



Misplacement of the opening of pencil-point needle could result in the deposition of anesthetics in the epidural space¹³.

Prevent the Needle Tip Displacement and Misplaced Injection



- ✓ The dorsum of one hand should be anchored firmly against the back of the patient and the fingers used to immobilize the needle, while the other hand is used to manipulate the syringe¹³



- ✓ Rotate the needle through 360° after the initial appearance of CSF and before aspiration, which may reduce the risk of the membrane edges catching on the opening of pencil-point needles¹³

Allow Sufficient Time for the Block to Establish

Inadequate time for the block to establish can precipitate pseudofailure of spinal anesthesia¹¹:

- ✓ Maximum time limit for the onset of action after drug deposition into the intrathecal space is 15-20 minutes¹¹
- ✓ Anesthetic is unlikely to produce desired action after this time period¹¹
- ✓ The slower the onset of either sensory or motor block, the more likely an inadequate block results¹¹



Assess the Block before Skin Incision

Formal testing of the block is recommended prior to commencement of surgery.
Three common modalities of the testing include¹¹:



**Sensation
of cold**
(ice cubes or ethyl
chloride spray)



Light touch
(cotton swab)

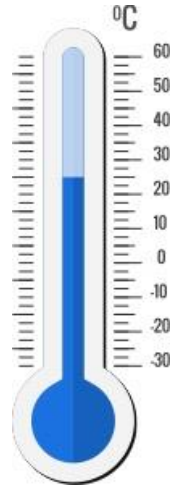


**Loss of
motor power**

Store the Anesthetic Agents Properly



Avoid prolonged
exposure to sunlight



Do not store
above 25°C



Do not freeze

Naropin (Ropivacaine)

Indication

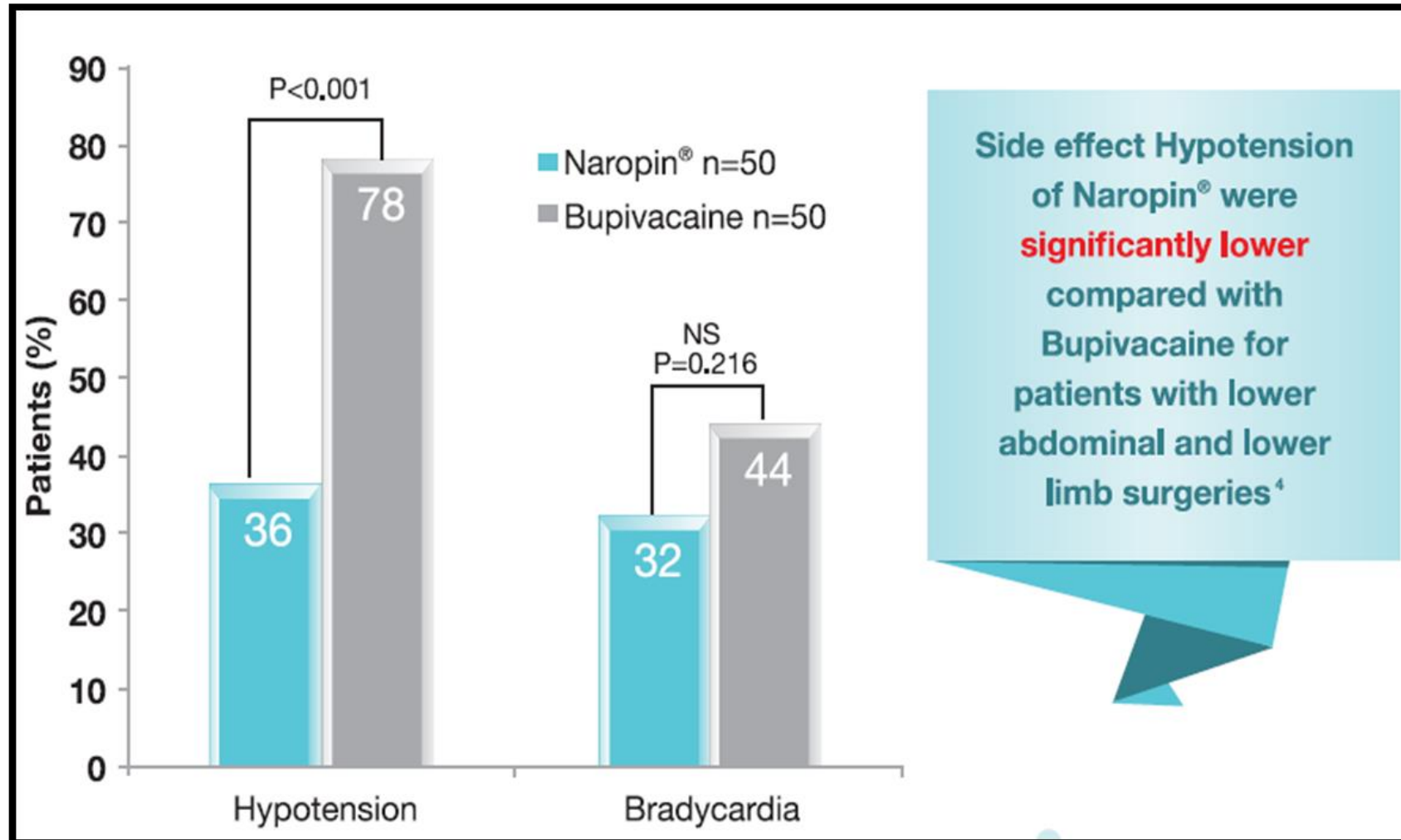
1. Anesthesia for surgery

- Epidural block, including cesarean section
- Peripheral nerve block and infiltration anesthesia

2. Acute Pain Management

- Continuous epidural infusion or intermittent bolus administration (postoperative or labor pain)
- Peripheral nerve block and infiltration anesthesia

Cardiotoxicity and CNS Toxicity



Cardiotoxicity and CNS Toxicity

- The incidence of cardiotoxicity and central nervous system (CNS) toxicity as a result of accidental intravascular injection of Ropivacaine appears to be low.
- According to an analysis of data collected from 3000 patients in 60 clinical studies, the incidence of possible accidental IV injection of Ropivacaine was 0.2% (six patients) and only one patient had a seizure; none of the patients showed any signs of cardiotoxicity.
- Convulsive local anesthetic doses of bupivacaine and ropivacaine were studied in different animal models; bupivacaine has a seizure threshold 1.5 to 2.5 times lower than ropivacaine. Based on animal and volunteer studies, it can be concluded that ropivacaine appears to be less neurotoxic and cardiotoxic than bupivacaine.

Dosage and Administration

	Const mg/ml	Volume ml	Dosage mg	Onset min	Duration hour
<i>Surgical Anaesthesia</i> <i>Lumbar Epidural Administration Surgery</i>	7,5	15-25	113-188	10-20	3-5
<i>Lumbar Epidural</i> <i>Administration Caesarean Section</i>	7,5	15-20	113-150	10-20	3-5
<i>Thoracic Epidural</i> <i>Administration To establish block for post operative pain relief</i>	7,5	5-15	38-113	10-20	n/a
<i>Field Block</i> <i>(e.g. minor nerve blocks and infiltration)</i>	7,5	1-30	7,5-225	1-15	2-6

Dosage and Administration

	Const mg/ml	Volume ml	Dosage mg	Onset min	Duration hour
Acute Pain Management					
Lumbar Epidural		10-20	20-40	10-15	0,5-1,5
Administration	2,0	10-15	20-30		
Bolus	2,0	(Interval minimal 30 min)			
Intermittent injections (top-up) (e.g. labour pain management)					
Lumbar Epidural					
Administration					
Continous infusion (e.g. labour Pain and posperative pain management)	2,0	6 - 14 ml/h	12-28 mg/h	n/a	n/a
Thoracic Epidural Administration					
To establish block for post operative pain relief	2,0	4 - 8 ml/h	8-16 mg/h	n/a	n/a
Field Block (e.g. minor never blocks and Infiltration)	2,0	1-100	2-200	1-5	2-6

Management of Postoperative Pain

Epidural administration

Ropivacaine is given epidurally (via the lumbar or thoracic route) for postoperative pain after abdominal (upper or lower) surgery, gynecology, orthopedics, and other surgeries.

a. After stomach surgery

The efficacy of epidural ropivacaine has been compared with intravenous morphine, epidural bupivacaine, and ropivacaine in combination with fentanyl.

Ropivacaine, with or without morphine, is more effective in postoperative pain relief than intravenous morphine alone.

b. After orthopedic surgery

Patients who had undergone hip arthroplasty had significantly more effective pain relief with epidural ropivacaine than with intravenous morphine (primary end point) and additional analgesia was given to more patients in the morphine group than in the ropivacaine group.

Pain Management

Patients' assessment of quality of analgesia at the end of treatment.

	Inadequate	Poor	Adequate	Good	Very good
Group R	0%	0%	16%*	26%	58%*
Group B	0%	0%	40%*	33%	27%*

A significant difference was noted between Group Ropivacaine and Group Bupivacaine as percentage of “adequate” and “very good”. Fisher exact test.

* $P < 0.05$.

The quality of analgesia with Naropin® were **significantly higher** compared with Bupivacaine for pain management patients with hip replacement³

Take Home Message

- ❖ Marcain as an **Original product** has a high quality and have a proven efficacy
- ❖ The packaging can **reduce the risk of infection** → Double sterile packaging
- ❖ Naropin as Original Ropivacaine have well tolerated, **effective** for surgical Anesthesia

