# Script for:
# Local Anesthetic Agents
# Surgery 101 Podcast
# Department of Surgery
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Hello, and welcome to another episode of Surgery 101. My name is Urooj Siddiqui, and I am pleased to be serving as a guest host this week! I am a fourth year University of Alberta Medical student just recently finishing an anesthesia elective here at the UofA. I'd like to recognize and thank Dr. Ronald Cheng for his input and feedback on this podcast.

The objectives of this podcast are to:

- Describe the pharmacology of local anesthetics
- Look at the different types of local anesthetics
- Highlight the different techniques used in local anesthesia
- Outline the toxicities associated with common local anesthetic agents
- Recognize the indications for and against the use of local anesthetics

How many of you have ever had to get stitches, a tooth pulled or a small lump removed? Needless to say these would all be very painful procedures were it not for some local anesthetic.

When applied to nerves, local anesthetics block the generation and propagation of action potentials. This essentially induces an absence of sensation in the nerve's distribution distal to the point of application. In regional anesthesia, local anesthetics are applied to large nerves or near the spinal cord to provide diminished sensation to a large area – such as a limb or lower segment of the body. If a small discrete portion of the body (i.e. tooth or incision/laceration) needs to be "frozen", the local anesthetics are applied more distally.

Local anesthetics have been in use since 1884 when Carl Koller demonstrated their ability to anesthetize the corneal surface. The agent used at that time was cocaine, originally isolated from the cocoa plant in 1856. This was the first local anesthetic agent and was originally applied topically. Procaine, a synthetic alternative to cocaine was not developed till 1904. Since then, the invention of the hollow needle and syringe as well as nerve stimulators and ultrasound machines have launched the fields of local and regional anesthesia to parallel the value of inhaled anesthetics.

Having an understanding of local pain control is essential for all fields of medicine. It is well documented that poor pain management can manifest itself as: tachycardia, hypertension, hypoxemia, increased smooth muscle tone, N/V, gastro-paresis, poor wound healing, urinary retention and decreased mobilization. These unwanted effects can

lead to pneumonia, PE/DVT and even myocardial infarction. These are all undesirable, but readily avoidable, consequences of pain.

So regardless of whether you're a family doctor taking skin biopsies, a pediatrician putting in an IV line, an ER doc placing a few sutures, or a general surgeon securing a chest tube – knowing which local anesthetics to use and when is paramount.

## Pharmacology

Local anesthetics work by binding to inactivated sodium channels on the nerve cell membrane. In doing so they are preventing sodium ion influx and subsequent membrane depolarization and action potential. Numerous theories have been proposed to more exactly explain their mechanism of action, including the critical volume hypothesis, surface charge theory, and surface receptor theory.

Potency of local anesthetics is related to their lipid solubility. Specifically, potency increases with increasing hydrophobicity of the local anesthetic (LA) molecule. Multiple measures of LA potency exist. Cm is the minimum concentration of LA needed to block nerve impulse conduction by 50%. Minimum Effective Anesthetic Concentration (MEAC) is the concentration of spinal anesthetic that produces surgical anesthesia within twenty minutes of administration in 50% of patients.

The onset of action of LA agents depends on multiple factors. The ratio of ionized water-soluble form and non-ionized lipid soluble form of the molecule is a big factor. The $pK_a$ of LA agents is the pH at which it is equally divided between its ionized and non-ionized form. LA's that have a $pK_a$ close to physiologic pH will have a higher concentration of their non-ionized form which can pass through the nerve cell membrane and produce a faster onset of action. This fact can be exploited as co-administration of bicarbonate with LA agents speeds the onset of the block.

## Types of LA agents

Local anesthetic agents are molecules made up of a lipophilic component and a hydrophilic component, both connected by an intermediate group containing *either* an ester or an amide group. The intermediate group is the basis for classification of the drug as either an ester or amide.

### *Amide-type LA's*

These are the ones we use most often. These molecules are broken down in the liver by cytochrome P450; breakdown metabolites are excreted in the urine. Examples of amide-type LA's include bupivacaine, dibucaine, etidocaine, lidocaine, mepivacaine, prilocaine and ripivacaine.

### *Ester-type LA's*

These molecules are broken down by plasma and hepatic esterases; metabolites are excreted by the kidneys into the urine. Examples of ester-type LA's include chloroprocaine, cocaine, procaine, and tetracaine. These agents tend to have more allergic reactions associated with their use.

One easy way to remember if a LA is an amide is if it's generic name has 2 i's it is an amide. If the generic name only has 1 i, it is an ester.

Both ester- and amide-type LA's can be applied using a variety of techniques, including epidural, caudal, and spinal infiltration, as well as peripheral nerve blocks and topically also.

## Toxicities

Toxicity from local anesthetic agents occurs when the drug is accidentally injected intra-vascularly, an excessive amount is given or there is an unexpected and rapid absorption of the agent. Because these agents block inhibitory CNS nerve fibers and then excitatory ones, the initial indications of systemic CNS toxicity are usually excitatory in nature. There are a variety of systemic indications of toxicity, all of which appear in a dose dependent manner. Common CNS side effects, in order of severity, include: perioral tingling and tongue numbness, tinnitus, visual disturbances, muscle twitches and tremors, loss of consciousness, seizures and convulsions, and finally coma and respiratory arrest in very extreme cases.

Cardiovascular indications of systemic LA toxicity include: vasodilation and hypotension, decreased myocardial contractility, prolonged PR and QRS intervals, bradycardia, dysrhythmias and finally cardiovascular failure in severe cases.

Part of the management of toxicity from LA is prompt and accurate identification of the event. As with any emergent situation, you must provide oxygen and secure the patient's ABC's. Further to this, medications such as diazepam or sodium thiopental may be given to increase the seizure threshold. Any arrhythmias present should be managed appropriately. Finally, you may also consider the administration of Intralipid 20% to facilitate binding of the excess LA still in circulation.

A commonly asked question in the OR's is what are the maximum doses of commonly used LA agents. For Bupivacaine it is 3 mg/kg. For Lidocaine it is 7 mg/kg with epinephrine and 4.5 mg/kg without epi.

## Indications & Contraindications

Indications for the use of a local anesthetic are quite broad. Overall, this includes the necessity of pain control/anesthesia for the completion of any surgical procedure. Conversely, the use of local anesthetic agents is limited by patient hypersensitivities, concurrent use of certain other medications, which may alter metabolism of the LA, and the presence of infection or inflammation at the injection site.

It is important to appropriately address the need for LA use but also to judiciously rule out any factors that may exclude their use.

## In Summary

1. Local anesthetics provide anesthesia and pain control by blocking generation and propagation of action potentials
2. LA agents are divided into two main subtypes, amide-type and ester-type, based on their intermediate molecular group
3. Local anesthetics can be applied in a variety of different ways to produces anesthetic effects
4. Systemic toxicity from LA agents is possible and is most likely to present with CNS and CVS signs and symptoms
5. Indications and contraindications should always be reviewed before using LA's