Differential Rates of Intravascular Uptake of Local Anesthetics

The rate of systemic absorption determines the peak plasma concentration of local anesthetics and the time to reach the peak concentration. *The systemic absorption rate correlates with the vascular supply* and the contact area between the local anesthetic and the vascular bed of the injected plane.
To mitigate the local anesthetic systemic uptake, adding **epinephrine** is one of the methods.

- Adjunctive epinephrine:
  - Slows the local anesthetic entry into plasma
  - Delays the uptake systemically
  - *Decreases the toxic effect on vulnerable tissues (cardiac and CNS).*
- *Decreased absorption* leads to
  - Increased neuronal uptake
  - Enhanced analgesia quality
  - *Prolonged the duration of action*
  - Limited toxic side effects
- **Shorter-acting local anesthetics have a greater effect when vasoconstrictors are used**. For example, the addition of epinephrine to lidocaine usually extends the duration of anesthesia by at least 50%. However, **epinephrine has little or no significant effect when added to *bupivacaine***, whose **long duration of action is due to a high degree of protein binding**.

LAST (**L**ocal **A**nesthetic **S**ystemic **T**oxicity) is a critical adverse event that may occur after a peripheral nerve block. Although the incidence of LAST associated with peripheral nerve blocks is decreasing owing to the use of ultrasound imaging, *seizure or cardiac arrest still occurs at an estimated rate of 2.6/10,000 ultrasound-guided blocks.*
Potency, onset of action, and duration of action are all closely correlated with the **lipid-solubility** of local anesthetics.
The **systemic absorption rate** is dependent on the site's **vascularity**.

- **Blood (intravenous) > tracheal > intercostal > caudal > paracervical > epidural > brachial plexus > subarachnoid/sciatic/femoral > subcutaneous.**

Esters are metabolized by pseudocholinesterase.
Amides are metabolized by microsomal P-450 enzymes in the liver.