function of blood concentration and free Xylocaine is found in the urine of humans in 6-11% of the total administered dose (Sung and Truant, 1954). Following oral doses of 5-7.5 mg./kg., it is still detectable in the urine after 6-8 hours. However, it is not detectable in the blood after two hours. Following intravenous doses of 4 mg./kg. in man, the Xylocaine blood levels after five minutes were found to be 5 micrograms/ml.

In spinal anesthesia with a total dose of 200 mg., the initial spinal fluid levels were found to vary between 3-5 mg./ml. spinal fluid. Surgical anesthesia becomes inadequate (60-80 minutes) when the spinal fluid level of Xylocaine declines to a concentration of 100-300 micrograms/ml. The addition of 0.3 mg. of epinephrine to 150 mg. of Xylocaine enhanced the duration of anesthesia by thirty minutes and maintained the spinal fluid level of Xylocaine at a level similar to that mentioned above (see Fig. 7).

The liver is the principal site for the biotransformation of Xylocaine. In partially hepatectomized rats, it was demonstrated that sleeping time was markedly increased and that the lethal effects of Xylocaine were somewhat increased. In these animals, because of the relatively high blood level of Xylocaine, its excretion by the kidney was increased. By the use of liver slices, it was possible to demonstrate the inactivation of Xylocaine. Its biotransformation was found to be oxygen dependent. However, the end products of metabolism have not yet been clearly elucidated.

The Administration of Local Anesthetic Drugs

Realizing that successful and uneventful regional anesthesia is to a large extent dependent upon a thorough understanding of the pharmacology of the local anesthetic drugs, the safeguards that must be practiced with their administration, and recognition of potential complications that accompany their use, as well as the ability to institute prophylaxis or adequately manage untoward reactions, the following summary of fundamental considerations for the administration of local anesthetic drugs is presented.

Selecting a Drug

The administrator must first consider the demands to be fulfilled by the local anesthetic drug in the problem for which the proposed anesthesia is to be used and the technique to be employed. Selection of a drug based on its properties and ability to meet these demands is then possible. The drug with the widest clinical utility and overall efficiency will most frequently answer the demands and thereby will be the most commonly used local anesthetic drug. The converse is true of drugs whose properties prevent their widespread utility. Careful selection is therefore dependent upon comparative evaluation of latency period, absolute and relative toxicity, potency and relative potency, anesthetic index, duration of effect, diffusion potential,

stability, surface activity, irritancy, sensitivity, compatibility, etc.

Epinephrine or another suitable vasoconstricting agent should be added to the anesthetic solutions, when indicated, to delay absorption and prolong the duration of the anesthesia. If epinephrine is selected, concentrations of 1:100,000 may be used, however, a concentration of 1:200,000 to 1:300,000 will provide the desired effect in most instances. Its use is contraindicated in medical problems such as diabetes, hyperthyroidism, peripheral vascular disease, hypertension, nephritis, cardiac disease; in extremity blocks distal to the wrist and ankle, and in surgery of the ear, nose, and penis, and when cyclopropane, chloroform, or ethyl chloride is used for supplementary anesthesia.

Administration

Correct administration of a local anesthetic agent demands considerably more of the administrator than the knowledge necessary for depositing the drug in the desired area. Foremost among these are the safeguards that must be enacted to prevent complications and sequelae that may accompany faulty techniques of injection of the local anesthetic. To this extent, the following are presented as the precautionary measures that are important in preventing a reaction.

A. *Use a minimal effective concentration.*

The lowest concentration of the local anesthetic that will produce the degree of blockade desired should be the maximum concentration used. Sensory analgesia with minimal motor fiber involvement may be obtained with dilute concentrations of the local anesthetic agent. Nerves of large diameter require proportionately higher concentrations of drug than those of small diameter.

When a mixed nerve is blocked, pain and touch fibers are blocked first, followed by sensation to heat and cold, while the motor fibers are the last to have their conduction impaired.

B. *Use a minimal volume of solution.*

The smallest volume of drug that is sufficient to adequately bathe all of the nerves supplying the area to be blocked should be the maximum volume used.

C. *Individualize total dosage.*

The administrator must always consider the age, physical status and size of the patient. The elderly and debilitated will not tolerate what may be considered an average dose of a local anesthetic without an increased incidence of systemic reactions. Obviously, a five foot, small-framed individual will require less volume of drug to effect a blockade of a specific field with peridural anesthesia than would a six foot, large-framed individual.

D. *Inject slowly and aspirate frequently.*

This is probably the most neglected or improperly performed safeguard associated with administration of local anesthetic agents. Injections should always be made slowly and aspiration should be done before and frequently during the injection of large volumes. The needle should be rotated in various planes and very gentle negative pressure applied.

It is not an infrequent occurrence to be unable to aspirate blood in one plane and freely aspirate it when the needle is rotated 90°–180°. It is also not uncommon to be able to aspirate pure blood after an injection of a few cc. of drug and an initial negative aspiration. The negative pressure applied by many administrators is often so great that the vessel wall occludes the bevel, preventing

aspiration. Gentle aspiration is imperative. Both slow injection and frequent aspiration provide safer anesthesia.

E. *Do not leave solution in metal containers.*

Local anesthetics react with certain metals and cause the release of their respective ions which, if injected, may cause severe local irritation. Adequate precaution should be taken to avoid this type of interaction.

F. *Personally identify the local anesthetic agent.*

It is extremely important that the administrator personally identify the agent to be injected. This may be done by withdrawing the drug solution from a properly labeled ampule or vial. Tasting the solution is an additional means of identification.

G. *Premedicate the patient.*

The importance of pre-anesthetic preparation of the patient with premedicant drugs is applicable to regional as well as general anesthesia. The value of the premedicants lies in their ability to minimize central nervous system excitatory reactions and to alleviate apprehension. Overpremedication will diminish the patient's ability to cooperate, which is of importance in performing most blocks. In the not too distant past, it was the accepted procedure to heavily premedicate individuals who were to receive regional anesthesia. This is no longer practiced by most anesthesiologists today who administer only the amount of premedication that they believe will achieve good psychic sedation. This usually consists of a barbiturate two hours before and a narcotic and cholinergic blocking agent one hour before surgery. Supplementary sedation is added as needed or indicated, using intravenous barbiturates. It is always better to act prophylactically

rather than therapeutically. Nevertheless, it should be remembered that barbiturates used prophylactically offer only a small degree of protection against a lethal dose of a local anesthetic.

H. *Closely observe the patient during and after injection for evidence of reactions.*

During injection, a patient complaining of headache, dizziness, or palpitation, necessitates slowing or temporarily discontinuing the administration. Sudden apprehension, pallor, nausea, tachycardia, clonic or tonic convulsions, or syncope are evidence of toxic blood levels. Frequent pulse and blood pressure recordings and close observation for progression of signs and symptoms will assure the administrator as to the advisability of continuing the injection. Diagnosis and treatment during the prodromal phase of a systemic reaction is of extreme importance.

I. *Be prepared to manage any emergency.*

It is imperative that the equipment and supplies necessary to manage any immediate untoward reaction to the local anesthetic agent be available for momentary use. To avoid being negligent and to be thoroughly prepared, the administrator must always be self assured that the following items are present and in operating order before injecting any local anesthetic.

1. *An apparatus for ventilating a patient with oxygen.* Oxygen supply alone is inadequate, as many times assisted or controlled ventilation is necessary. An anesthetic machine is preferred, and may be used for general anesthesia in the event that the block is unsuccessful.
2. *Airways.* Nasal and pharyngeal airways are a necessity, and endotracheal equipment is advised; the operator should be skilled in its use. The unconscious patient often needs an airway to permit ventilation and bypass obstructions.

3. *An infusion set.* A bottle of intravenous fluids and the equipment necessary for administration should be readily available. This should be started as soon as adequate ventilation is assured.
4. *An intravenous barbiturate.* There should always be available a solution of a short or ultra-short acting barbiturate as well as a syringe and needle. Should convulsions occur, very small increments of a barbiturate (i.e., thiopental, I.V. 30–50 mg./min.) or a muscle relaxant should be injected. Only the dose necessary to stop convulsions should be used, since local anesthetics cause medullary depression with overdosage and the barbiturate will potentiate this action.
5. *A vasopressor.* A vasopressor drug should be available for adding to the infusion whenever circulatory collapse occurs. Levarterenol bitartrate and phenylephrine hydrochloride are the more commonly employed drugs. However, if the collapse is mild, such drugs as ephedrine sulfate, methoxamine hydrochloride, methamphetamine hydrochloride, etc., may be used in small increments to support the circulation.

J. *Discard solutions containing aspirated blood.*

Clinical Application of Local Anesthetics

The properties of Xylocaine as previously described indicate that this drug very closely approaches the desired qualities of an ideal local anesthetic drug. The generalized acceptance of Xylocaine by both the medical and dental professions is directly attributable to its widespread clinical utility. Its ability to withstand prolonged storage and autoclaving without loss of potency permits the anesthesiologist to be confident that the agent has maintained its effectiveness. Xylocaine may be used either topically or by injection methods. It is capable of producing regional anesthesia by abolishing conduction of afferent and efferent impulses at any point along their nerve pathways. Its property of tissue penetration, wide margin of safety, and unusually low tissue irritancy makes Xylocaine a local anesthetic of choice for conduction anesthesia.

Surface Anesthesia

Xylocaine produces rapid and effective anesthesia of the mucous membranes of the respiratory, upper gastrointestinal, and lower genito-urinary tract, the eye and ear, and the ano-rectal area. It is also effective when topically applied to the broken skin for pain or burns and abrasions, for open wounds and pruritis. It is non-irritating and well tolerated.

Four preparations of Xylocaine are available for surface use: (1)