prophylaxis and therapeusis of cardiac arrhythmias during cardiac surgery and the treatment of epileptic states by intravenous Xylocaine HCl.

In 1956 Carden and Steinhaus showed that Xylocaine HCl was effective in both normothermic and hypothermic dogs when used directly into the left ventricle in connection with cardiac resuscitation from ventricular fibrillation. Also in 1956, Harris *et al* demonstrated the effects of Xylocaine HCl upon ventricular tachycardia resulting from myocardial infarction in the dog.

These findings, have, in recent years, been transferred into human open-heart surgery, and thus, Hitchcock *et al* (1958, 1959) have shown Xylocaine HCl to be effective in many types of cardiac arrhythmias, both mechanically and non-mechanically induced.

Specifically, as shown by Likoff (1959), premature systoles, paroxysmal supraventricular tachycardias, and paroxysmal ventricular tachycardias have responded well to the intravenous use of Xylocaine HCl.

The problems involved in the treatment of epileptic states have always been a challenge to all investigators. Bernhard *et al* (1955) and Bohm *et al* (1959) have shown that Xylocaine HCl is of great use in the treatment of status epilepticus. It was also found that a barbiturate in doses too small to influence the epileptic attack increases the anticonvulsive effect of Xylocaine HCl. Since the supplementary dose of the barbiturate can be kept so low that the complications of its sedative effects are avoided, this combination therapy is recommended in the treatment of severe status epilepticus.

Thus, by considering the four areas of applicability for intravenous Xylocaine HCl, it can be seen that these technics and this agent have introduced to medical science a new concept of therapy in many fields.

Complications and Sequelae Related to the Local Anesthetic Agents

The administration of drugs by injection always presents a number of potential problems and possible sequelae. Once administered, they cannot be removed, and specific antagonists are seldom available. Tolerance and sensitivity are varied. Control of the drug in regards to distribution and elimination is not always possible and therefore the results not consistently predictable. The administrator must institute proper prophylaxis and be prepared to manage any untoward reaction that might occur.

SYSTEMIC REACTIONS

This is unquestionably the most common complication associated with the administration of local anesthetics. Systemic reactions almost invariably result from high blood levels, but are on very rare occasions due to allergy. These may occur with topical application or with injection. These reactions must also be differentiated from a systemic reaction due to vasoconstrictor drugs.

High blood levels.

High blood levels of the drug accumulate from one or more of the following mishaps; (1) overdosage, (2) rapid absorption, and (3) slow distribution, elimination or destruction. Rapid blood stream accumulation may be due to inherent properties of the drug, injection into a vascular area, and failure to use a vasoconstrictor. Failure

of the body to eliminate the drug may also be due to the properties of the drug or to physiopathological states present that prevent its removal from the blood stream. Reactions due to overdosage are preventable, and their elimination alone would markedly reduce the incidence of this complication.

Prophylaxis. Use drug with a high anesthetic index: The anesthetic index may be used for selecting a local anesthetic drug with the widest margin of safety. A drug having an index higher than procaine or cocaine is considered to have a wider margin of safety. This in substance means a drug that offers minimal opportunity for accumulation of toxic blood levels when minimal effective concentrations are used and due precautions are exercised.

Use minimal effective concentrations: The toxicity of the different local anesthetic drugs increases in varying degrees with changes in concentration. The more dilute the solution, the larger the volume of solution tolerated. The more concentrated solutions necessitate using considerably smaller volumes. It must be remembered, however, that large nerve trunks require higher concentrations than smaller nerves, and the latter in turn require stronger concentrations than is necessary for infiltration (see pages 56 and 57).

Limit total dosage: Laboratory data and clinical trial has substantiated a maximum recommended dose for each of the accepted local anesthetic agents. It is advisable that less than this amount be used when a vasoconstrictor drug is not added. Special consideration should be given to the aged and debilitated, as well as to children, and to patients with liver damage.

Be cautious when injecting vascular areas: Vascular areas mean rapid absorption and hence a constant possibility of high blood levels. This is particularly true when the total dosage to be injected is high. Examples of vascular areas where the highest incidence of high blood levels occur are the face, neck, scalp, penis, and peridural space (particularly the caudal canal).

Use a dilute solution of epinephrine when its use is not contraindicated.

Clinical Manifestations. Recognition of the early signs of a systemic reaction will result in more effective management. If the reaction is allowed to progress to the advanced or delayed phase, morbidity and mortality will rise proportionately.

Central Nervous System

Stimulatory Phase (early)

Cerebral cortex: Evidence of cortical irritability with apprehension, nervousness, and muscle twitching beginning in the face and limbs that may progress to convulsions.

Medulla: The medullary centers are stimulated, as demonstrated by increase in blood pressure and pulse, tachypnea, and nausea and vomiting.

Depressed Phase (late)

Cerebral cortex: unconsciousness, loss of reflexes and muscle paralysis.

Medulla: Depression of the medullary centers results in a fall in blood pressure due to cardiac depression and vasodilatation, absence of palpable pulse, and respiratory abnormalities to the extent of apnea.

Cardiovascular System

Direct depression of the myocardium and peripheral circulatory collapse may occur independently of or combined with central nervous system depression.

Xylocaine HCl does not follow the above pattern in regards to

stimulation of the central nervous system with increasing blood levels. The early sign of a high blood level is that of drowsiness with the patient capable of a conscious response to stimuli. This somnolence progresses with the increase in blood stream concentration until evidence of conscious cerebration is unobtainable. Central nervous system stimulation and subsequent depression coupled with cardiovascular depression then resemble reactions to other drugs.

Treatment. The equipment necessary to competently manage a systemic reaction should be in the immediate vicinity of the place where any local anesthetic is being administered.

Assure adequate ventilation of the patient: Maintain a patent airway, and administer oxygen using assisted or controlled ventilation as indicated. This would necessitate having available an apparatus with a reservoir bag and mask plus an oxygen supply. Start intravenous fluids: This assures immediate and continued access to the vascular system.

Stop convulsions: This may be managed by the intravenous injection of small increments (30-50 mg.) of thiopental sodium. Refrain from using unnecessary amounts because of its additive effect on any cardiac or central nervous system depression present or resulting from toxic blood levels of the local anesthetic agent.

Support the circulation: Vasopressors may be used as indicated to maintain peripheral resistance.

Restore cardiac function: Manual systole may be found necessary if the reaction is allowed to progress with inadequate management. Asystole or ventricular fibrillation may be an early development in the diseased heart or when a high blood level has developed rapidly.

Observe the patient until recovery is assured.

Drug Idiosyncracy.

A relatively small percentage of reactions result from intolerance to local anesthetics. It is probable that many of the reactions associated with overdosage may also be reacting from intolerance, and are therefore unrecognized. This diagnosis is possible only when a small dose of only the local anesthetic is administered and no other agents are in effect.

Prophylaxis. Question patient in regards to previous untoward reactions with local anesthetics.

Perform tests such as skin wheals, patch, and mucous membrane tests. This is practical only when patients have a history of previous difficulty with local anesthetics, and their value has been questioned.

Clinical Manifestations.

Generalized urticaria.

Generalized angioneurotic edema with difficulty in ventilation.

Pruritis.

Hypotension, which may progress to circulatory collapse.

Myocardial depression which may progress to asystole.

Nausea and vomiting.

Profuse sweating.

Unobtainable pulse and blood pressure.

Treatment. Antihistaminic drugs: Diphenhydramine hydrochloride, 60 to 100 mg. intravenously (slowly).

Epinephrine: 0.25 to 0.5 cc. of 1:1000 concentration intravenously (slowly).

Maintain airway and administer oxygen with bag and mask as indicated.

Start an intravenous infusion containing a vasoconstrictor.

Reactions to Vasoconstrictor Drugs.

Reactions resulting from vasoconstrictor drugs are due almost entirely to high blood levels. The reaction resembles the early stimulatory phase of a local anesthetic reaction, and as a result the anesthetic is most often blamed for what is actually a reaction to the vasoconstrictor.

Strong concentrations of epinephrine and other vasoconstrictors are used in dental blocks because of the highly vascular area where the agent is deposited. Epinephrine prolongs absorption and allows the anesthetic agent time to establish and maintain a blockade. It is also used to prevent occurrence of high blood levels of the local anesthetic. A large percentage of patients absorb the vasoconstrictor in sufficient amount to experience palpitation, tremors, etc., and believe they have reacted to the local anesthetic.

Reasons for use.

Prolong anesthesia. Reduce rate of absorption of the local anesthetic. Bloodless field.

Clinical manifestations.

Headache. Palpitation. Hypertension. Tachycardia. Pallor. Tachypnea. Tremor. Anxiety and fear. Nausea and vomiting.

Treatment. Small dosages (30-50 mg.) of thiopental sodium intravenously if the reaction is severe and the patient is not unconscious. Adrenolytic drugs such as dibenamine hydrochloride in small intravenous dosages may be considered if the reaction is prolonged and severe.

The majority of systemic reactions are preventable. To minimize the incidence, all safeguards should be practiced with each administration.

LOCAL REACTIONS

Tissue reactions at the site of injection are not uncommon and are related to properties of the individual drug or to faulty technics.

Reactions related to local anesthetic agents.

Slough of Tissue. The irritancy of certain drugs to human tissue causes inflammatory reactions that are at times severe enough to cause tissue necrosis and a resultant slough. Xylocaine HCl has been shown to be the least irritating of the commonly used local anesthetic. (see pages 32 and 36).

Irreversible nerve damage. The use of unnecessarily strong concentrations, drugs with high irritancy, or the use of drugs such as phenol and alcohol may produce irreversible damage to nerve tissue with residual neurological sequelae.

Swelling of tissues. This is attributed to the injection of metallic ions that are released by the effect of certain chemical disinfectants on metal receptacles, such as syringes and needles.

Reactions related to faulty technics of injection.

Reactions in this area are usually attributable to the use of improperly sterilized equipment and solutions, and/or to the use of wrong compounds.