

Despite their similar molecular size, prilocaine is excreted faster than lignocaine. The renal excretion rate is influenced by the disposition of local anaesthetic drugs in whole blood and their dispersal in peripheral tissues. Neither lignocaine nor prilocaine affects renal haemodynamics (Eriksson et al 1966).

4. SYSTEMIC EFFECTS OF LOCAL ANAESTHETIC AGENTS.

A. CARDIOVASCULAR EFFECTS OF LOCAL ANAESTHETIC AGENTS.

In the normal patient the cardiovascular system is not as sensitive to the toxic effects of circulatory local anaesthetic drugs as the central nervous system. However, in certain circumstances, the cardiac effect is probably the more serious (Steinhaus 1957, Moore 1955).

Heart disease is increasing. With people living longer, an increasing number suffer from degenerative heart conditions of old age (ADA and AHA 1965); yet, because of advances in medical science, many are able to lead an apparently normal life (Schirger et al 1967, Morris 1967). The incidence of all forms of congenital heart disease in Australia is one in 200 live births (Hall 1967). It is important therefore that the dentist ascertain his patient's cardiovascular status as the existence of heart disease may predispose the myocardium to the direct depressant action of local anaesthetic drugs. In dentistry, the latter effect

is most likely to be manifested as a result of inadvertant rapid intravenous injection. In addition, myocardial weakness is accentuated by anoxia or hypoxia (Gordh 1965). Because the cardiac response to rapid intravenous injection of local anaesthetic drugs is immediate and may lead to total cardiovascular collapse, Steinhaus (1957) considers it to be more serious than the central nervous system effects which are of a slower progressive nature. Although rapid intravenous injection may result in cardiovascular collapse due to the direct depressant effect of local anaesthetic agents on the myocardium, oxygen want is the main cause of heart failure which occurs in the penultimate stage of systemic toxic reaction to local anaesthetic drugs. Several types of oxygen want are then present. Firstly there is tidal hypoxia due to the decrease in respiratory exchange which follows depression of the medullary respiratory centre by local anaesthetic agents. It seems reasonable to assume also that when the cerebral cells are initially stimulated by local anaesthetics, their oxygen requirements are increased, and if this need is not met, a demand hypoxia follows. Finally there is stagnant hypoxia due to the slowed circulation (Moore 1955).

The cardiovascular effect of high plasma concentration of local anaesthetic drug is a summation of the individual effects on the heart and blood vessels (Foldes and

McNall 1961). These effects occur either by (a) the direct peripheral action of the local anaesthetic drug or (b) are mediated indirectly via the central nervous system.

(a) peripheral cardiovascular effects of local anaesthetic drugs.

When applied directly in sufficiently high concentration, local anaesthetics affect the myocardium producing a decrease in electrical excitability, a decrease in conduction rate and a decreased force of contraction (Goodman and Gilman 1966, Foldes et al 1960, Wiedling 1964).

Depending on the rate of infusion, local anaesthetic drugs administered intravenously may have an initial stimulatory effect on the circulation which is centrally mediated (Moore 1955). However, all synthetic local anaesthetics administered intravenously have an early, direct depressant effect on the myocardium (Sara 1963), and may also produce sympathetic blockade with resultant bradycardia (Sadove 1952).

In the peripheral vasculature, local anaesthetic agents cause direct depression of the smooth muscle component of the blood vessel wall and also may depress sensory receptors thus abolishing local reflex tone (Goodman and Gilman 1966). The result is vasodilatation. When, as a result of high plasma concentration of local anaesthetic

drug, bradycardia and vasodilatation occur simultaneously, extreme hypotension ensues (Adriani and Campbell 1956), and if this trend is not reversed, the heart will fail as a result of oxygen want (Wolcott 1963).

Although oxygen want is the primary condition during systemic reaction to local anaesthetic drugs, and cardiovascular collapse is secondary; the direct action of these drugs on the heart cannot be completely ignored as contributing to heart failure (Steinhaus 1957, Steinhaus 1962, Gordh 1965, Adriani and Campbell 1956). Primary cardiovascular collapse and death have occurred from small doses of local anaesthetic probably as a result of rapid intravenous administration. Signs of central nervous system stimulation were absent and the response so abrupt as to rule out central nervous involvement (Moore 1955). The cause of the collapse is unknown, but may be due to a direct effect on the pacemaker or to the sudden onset of ventricular fibrillation (Goodman and Gilman 1966).

When systemic toxic reaction due to high blood level of local anaesthetic agents starts, there may be no initial variation in pulse rate and blood pressure from that determined prior to injection (Englesson et al 1962, Moore 1955). However, as previously mentioned, continuous intravenous infusion of local anaesthetic agents, and particularly the amides, has an initial stimulatory effect on the cardiovascular system which is manifested as an increase in pulse

rate and blood pressure due to stimulation of the medullary cardiovascular centre (Foldes et al 1960, Foldes et al 1965, De Jong and Walts 1966, Moore 1955). Following continuous intravenous infusion of local anaesthetic agents, electrocardiographic tracings indicative of deteriorating cardiac activity were encountered more frequently with ester type local anaesthetics than with amides (Foldes et al 1960). The latter exhibited only evidence of sinus tachycardia (Foldes et al 1965, De Jong and Walts 1966). However, the part played by the demand hypoxia which follows increased cellular activity, plus the tidal hypoxia due to respiratory depression must be regarded as contributing to blood pressure rises and tachycardia (Moore 1955).

As the toxic effect of local anaesthetic drug on the medullary respiratory centre progresses to depression, respiratory failure is evidenced by an alteration in respiratory rhythm and rate, coupled with an elevated pulse rate and blood pressure. Primary oxygen want develops mainly as the result of depression of the medullary respiratory centre, although depression of the medullary cardiovascular centre with resultant loss of peripheral vascular tone and bradycardia also contribute. The blood pressure remains elevated but the pulse slows and is full and bounding (Dobbs and Kader 1950). Cardiovascular collapse does not necessarily

accompany, precede, or follow respiratory failure. However, oxygen want often leads to hypotension and if this is not corrected, the skin becomes clammy and possibly cyanotic. Pulse rate gradually increases though decreased in volume and finally trails off into tachycardia before disappearing (Dobbs and Kader 1950). As a result of the peripheral vascular collapse, cerebral anaemia and syncope supervene (Moore 1955).

From a dental point of view, it is important to note that the early cardiovascular effects of both local anaesthetic and vasoconstrictor agents may be similar. Both elevate pulse rate and blood pressure and may produce arrhythmias. The other important cardiovascular effect of local anaesthetic agents is their direct depressant effect on the myocardium when administered rapidly intravenously; an effect which may be accentuated when the heart has been sensitized by disease processes or hypoxia.

B. CENTRAL NERVOUS SYSTEM EFFECTS OF LOCAL ANAESTHETIC AGENTS.

The characteristic pharmacological action of local anaesthetic drugs is convulsive, and respiratory and circulatory depressive (Steinhaus 1962, Gordh 1963). The convulsions which attend systemic toxic reaction due to high plasma concentration of local anaesthetic are usually attributed to overstimulation of the cerebral cortex.

although recent investigations suggest that regions of the temporal lobe other than the cortex, may be the site of focal seizure activity (De Jong and Walts 1966). However, convulsions may also be the result of hypoxia, or of both these causes (Moore 1955). In either case, the convulsions are the result of the effects of local anaesthetic agents on the central nervous system.

Local anaesthetics stimulate the brain from above downwards, affecting first the cortex and then the vital medullary centres of respiration and circulation (Epstein 1958, Moore and Bridenbaugh 1961).

The onset of systemic toxic reaction to local anaesthetic drugs may be immediate or delayed. The delayed type of reaction takes the form of a slow progressive deterioration of the patient's condition over a period of from 5 to 30 minutes and is caused by a slow build up of plasma concentration following the absorption of large amounts of drug. Reference to Table I indicates that particular care is needed in the administration of concentrated solutions of local anaesthetic without the benefit of a vasoconstrictor to delay absorption.

The systemic effects produced depend on plasma concentration of drug and as this increases, a spectrum of central nervous system manifestations is seen which commences with sedation (and occasionally excitation), and

progresses through anti-convulsant action to fine tremor activity, grand mal seizures, and culminates in loss of consciousness (De Jong and Walts 1966). With the anilide local anaesthetics the stimulatory phase may be slight and overlooked. Patients receiving lignocaine in doses exceeding 500 mg, may experience central depression and temporary loss of consciousness with no other signs of toxic reaction (Goodman and Gilman 1966, Moore 1955, Epstein 1958).

Stimulation of the cerebral cortex may be motor or sensory or a combination of both. Sensory stimulation produces sweating, restlessness, nervousness and loquacity. Motor cortical stimulation produces twitching, tremors and choreaform movements (Sadove 1952, Dobbs and Kader 1950, Spiro 1966). Accordingly, stimulation of the cerebral cortex may be manifested in signs such as sweating, muscle fasciculations, twitching, convulsions; and in subjective changes such as numbness of the face or extremities; sensation of twitching; difficulty in breathing, speaking or swallowing; blurred or double vision; dizziness, drowsiness; sensations of hot or cold; euphoria; disorientation and loss of consciousness. Those underlined are observed most often (Foldes et al 1965). The patient is frequently aware of a sensation of twitching before it becomes apparent and twitching of the facial muscles often

precedes actual convulsions (Toogood 1960). If the reaction is slight in intensity it may not progress past the stimulatory phase and is easily overlooked (Sadove 1952).

Cocaine's powerful stimulatory effect on the cerebral cortex is readily manifested in convulsions (Adriani and Campbell 1956). The amide local anaesthetics more frequently produce drowsiness or sedation than excitation; though generalized seizures are seen with these drugs (Englesson 1962, Foldes et al 1960, Foldes et al 1965, De Jong and Walts 1966, Sadove 1965, Truant 1965). Mepivacaine appears to have more convulsive effect than lignocaine. Its retarded toxicity may be due to slower absorption and, like lignocaine, it is slowly metabolized so that repeated administrations tend to be cumulative (Knox et al 1961, Le Chat and Deleau 1961, Englesson 1962).

Some doubt has been thrown on the accepted idea of convulsions originating from overstimulation of the cerebral cortex. No correlation has been demonstrated between the incidence of convulsions and changes in electroencephalographic recordings of cortical activity, in patients receiving continuous intravenous infusion of local anaesthetic drugs (Foldes et al 1960, Foldes et al 1965, Englesson et al 1962). The paroxysmal bursts typically seen in EEG tracings at seizure threshold, were absent. In fact the tracings

simulated the pattern of those of a person when normally asleep. De Jong and Walts (1966) demonstrated that lignocaine can be titrated to give rise to a well localized electrical temporal lobe seizure. They propose that many of the convulsive manifestations of local anaesthetics are attributable to focal seizure activity in the amygdala-hippocampal complex of the temporal lobe and not in the motor cortex as previously believed. This would explain the lack of activity previously noted in cortical EEG tracings at seizure threshold.

The medullary vomiting centre may be stimulated by toxic plasma concentration of local anaesthetic drug, and also as a result of the hypoxia which inevitably accompanies interference with the two systems which are vital for the absorption and transportation of oxygen; viz the respiratory and cardiovascular systems. Syncope, of whatever origin, is always associated with cerebral anaemia. Reflex inhibition of the cardiovascular system of psychogenic origin is a common cause of cerebral hypoxia. Accordingly, nausea and vomiting may occur either early or late in the course of systemic toxic reaction to local anaesthetics and do not necessarily indicate its severity (Moore 1955).

Similarly convulsions also may be attributed to the analeptic effect of local anaesthetic agents, to epilepsy,

or to any of the factors or complications associated with syncope (see Chapter IV), (Sara 1963). Therefore, like nausea and vomiting, convulsions do not necessarily indicate the severity of the reaction (Toogood 1960). However, during convulsions the oxygen requirements of the body are increased as a result of the violent muscular activity (Steinhaus 1952), and at the same time there is circulatory and respiratory depression (Sara 1963). The resultant oxygen want is often manifested in cyanosis.

Pharmacologically, in all cases of toxic reaction to local anaesthetic drugs, there is overstimulation to the point of depression (Sadove 1952). The depression is proportional to the degree of stimulation. Loss of consciousness is generally attributed to depression of the cerebral cortex following its previous overstimulation. However, it is possible that anaesthetic drugs depress the arousal centre in the reticular formation as well as specific cortical centres (Livingston 1953).

Although first the cortex and then the medulla are involved in systemic reaction to local anaesthetics, their stimulation and depression may be going on simultaneously with either predominating (Moore 1955). Signs of cortical stimulation are a warning that toxic reaction exists and may progress to central medullary paralysis. Cortical

stimulation presents a patient difficult to control whereas medullary paralysis is characterized by flaccidity and relaxation (Sadove 1952, Dobbs and Kader 1950). The degree of medullary depression which follows its overstimulation, depends on the speed with which the stimulatory phase is recognized and treated (Moore and Bridenbaugh 1961, Moore and Green 1957).

The part played by increased cellular metabolism following stimulation has been mentioned as contributing to cerebral hypoxia (Moore 1955). However, the commonest cause of oxygen want in toxic reactions to local anaesthetics is respiratory difficulty (Sara 1963).

Stimulation of the medullary respiratory centre by local anaesthetic drugs is occasionally manifested in the early stages of the reaction by an increase in rate and depth of respiration (Foldes et al 1965, Moore 1955, Foldes et al 1960). However, in the investigations of Foldes et al (1965), the direction of the early respiratory response following continuous intravenous infusion, seemed to depend on the toxicity of the local anaesthetic agent. Those local anaesthetics which, because of their rapid metabolism are generally regarded as possessing a low degree of systemic toxicity (viz:- procaine, 2-chloroprocaine and possibly meprylcaine), exerted a stimulatory effect on the respiratory

rate. The more toxic compounds lignocaine, mepivacaine, and isobucaine, tended to depress respiration. Depression of the respiratory centre follows in almost all cases of severe toxic reaction to local anaesthetic drugs and, depending on its severity, is manifested as irregular respiratory rate and excursion, sighing, dyspnoea, periods of apnoea and finally complete respiratory arrest (Moore 1955, Goodman and Gilman 1966). The direct effect of the local anaesthetic agent on the voluntary muscles of respiration also contributes to respiratory paralysis (Sara 1968).

The resultant oxygen want is the main cause of the cardiovascular collapse which follows respiratory arrest (Wolecott 1963). It has been demonstrated in animals receiving continuous intravenous infusion of local anaesthetic drugs that, provided adequate respiration is maintained artificially, the heart does not fail merely because of respiratory paralysis. When death finally occurs after the administration of many times the normal lethal dose, it is due to the direct depressant action of the local anaesthetic agent on the myocardium (Taintor and Throadson 1938, Gordh 1965).

The foregoing is an account of the sequence of events accompanying the delayed type reaction which follows gradual toxic accumulation of local anaesthetic in the blood stream.

Abrupt onset of reaction, on the other hand, is usually the result of either rapid intravenous administration or of rapid absorption of large amounts of local anaesthetic into the blood stream from regions of extreme vascularity (Adriani and Campbell 1956).

When local anaesthetic agents gain access to the blood stream rapidly, prodromal manifestations are absent and the classic overt signs of local anaesthetic toxicity are compressed into a short space of time and apparently occur simultaneously (Sara 1963). There is no slow deterioration of the patient's condition as the full impact of the intravenous dose of local anaesthetic is immediately felt on the heart before it is circulated to the usually more sensitive central nervous system. However, the immediate effect on the heart may result in primary cardiovascular collapse, particularly when the heart has been weakened by disease or hypoxia (Steinhaus 1952). In these circumstances, the cardiovascular effects of local anaesthetic agents are more serious than their central effects.

The high degree of intravenous potency of contemporary anilide dental local anaesthetic preparations is again emphasized. It is a simple matter to attenuate this toxic potential by ensuring that solutions are deposited slowly, extravascularly. This can only be accomplished with certainty by adopting preliminary aspiration as an integral part of routine local anaesthetic procedure.

SUMMARY AND CONCLUSIONS

Those properties of local anaesthetic and vasoconstrictor drugs, together with aspects of their administration, which contribute to the systemic toxicity of dental local anaesthetic preparations, have been reviewed. An evaluation of the problem of systemic toxic reaction under dental local anaesthesia can now be made.

It is difficult to give an accurate assessment of this aspect of local anaesthesia because much that has been written on the subject is based on conjecture. However, factual answers can be given to some of the questions related to local anaesthetic systemic toxicity, particularly those associated with intravenous injection. In other cases, it still remains for the dentist, through an intelligent appreciation of the signs presenting, to interpret his own clinical observations.

An attempt should always be made to determine the nature of systemic disturbances accompanying dental local anaesthesia. It would be advantageous if case reports of such reactions could be submitted to a special committee for analysis and comment, as well as for record purposes.

Just how common systemic disturbances under dental local anaesthesia are, is impossible to determine. Anyone who administers enough local anaesthetics will occasionally

observe evidence of their systemic toxic effects. Perhaps, the best preventive measure is an awareness that local anaesthetic preparations are potentially toxic. Certainly, systemic toxic reactions are more common than frequently assumed, as they are rarely reported in the literature either because of reluctance or indifference on the observer's part.

The ability of dental local anaesthetic preparations to elicit manifestations of systemic toxicity has been established, but the exact manner in which this occurs, particularly with the more common minor systemic disturbances, is not always clear.

At usual dental dosage, local anaesthetic or vasoconstrictor drugs gaining access to the blood stream in the desired way by gradual absorption from the injection site, seldom attain an equilibrium concentration which amounts to a toxic plasma level of drug. A delayed reaction of this type due to a slow build-up of local anaesthetic agent in the blood stream, takes from 5 to 30 minutes to develop and is rarely seen in dental practice. Furthermore, it requires the administration of quantities of drug which, depending on individual susceptibility, amount to a toxic overdose. However, it is impossible to designate limits of dosage as these vary from patient to patient and even in the same patient at different times.

Factors which influence dosage, such as the physical condition and emotional state of the patient, and the existence of pathological conditions or concurrent drug regimens which could cause an abnormal response to local anaesthetic or vasoconstrictor drugs, should be ascertained by pre-anaesthetic evaluation. This requires observation of the signs presenting and the taking of a relevant medical history.

Large volumes of solution containing toxic amounts of local anaesthetic and vasoconstrictor drugs are sometimes administered in dental practice. Furthermore, when concentrated solutions of local anaesthetic drugs are used without the benefit of a vasoconstrictor to delay absorption, special attention should be paid to the mass of drug administered, so that toxic accumulation in the blood stream is avoided.

It has been demonstrated that, when local anaesthetics are absorbed and enter the blood stream rapidly, the plasma concentration curve is similar to, though less than, that which follows rapid intravenous injection. However, no careful study has been made of the rate at which local anaesthetic preparations are absorbed from the various oral injection sites, nor of the plasma concentrations which are subsequently attained. Neither has there been any

detailed investigation of the incidence and type of reaction under dental local anaesthesia.

Consequently when systemic disturbance follows the extravascular use of local anaesthetic preparations, one can usually only speculate as to the cause, bearing in mind that the potential to cause systemic toxic reaction is inherent in the solution administered, while there is also probably a strong psychological element involved.

Usually only the beta effects of dentally administered adrenaline are observed following absorption from the injection site. These same effects accompany the release of endogenous adrenaline into the blood stream in response to sympathetic outflow, the most important of which is its property of decreasing peripheral resistance. In this way adrenaline regulates cardiac output by increasing venous return.

Loss of tone or collapse in the peripheral circulation due to psychological causes or the direct effect of local anaesthetic drugs, decreases venous return, producing hypotension. In addition, the heart may be depressed by either of these causes, producing bradycardia. While the effect on the heart of sympathetic outflow and sympathomimetic drugs is stimulatory, parasympathetic activity

and local anaesthetic agents inhibit cardiac action. However, local anaesthetic agents may have an early stimulatory effect on the heart similar to that of vasoconstrictor agents.

When attempting to use blood pressure and pulse rate recordings as diagnostic aids in determining the cause of minor systemic disturbances under dental local anaesthesia, it is difficult to differentiate between those manifestations which are due to local anaesthetics, those due to vasoconstrictors, and those which are of psychogenic origin.

When local anaesthetic agents and vasoconstrictors gain direct access to the blood stream as a result of rapid intravenous injection, the cardiovascular system is directly affected. One of the most dramatic sights in all pharmacodynamics is the pressor response which follows intravenous injection of minute amounts of adrenaline. When administered together, the local anaesthetic agent may increase the brief drop in blood pressure which follows the initial rise due to intravenous injection of adrenaline. Both agents may stimulate the cardiovascular system and produce arrhythmia. However, plain local anaesthetic agents administered rapidly intravenously, usually have a strong direct depressant effect on the heart and blood vessels, producing bradycardia, vasodilatation, hypotension, or even cardiac arrest.

The vasoconstrictor agent has little effect on the central nervous system except that mediated via changes in the cardiovascular system. In the normal individual the central nervous system is more sensitive to the toxic effects of local anaesthetic agents than the cardiovascular system. Individual susceptibility plays an important part as regards uptake of local anaesthetic agents by the central nervous system, and the resultant toxic manifestations produced. These may be respiratory and circulatory depression, or convulsions.

Rapid intravenous injection produces a concentrated depot of drug within the blood stream, which has the opportunity of influencing the carotid and aortic receptor sites as well as the heart and central nervous system.

The use of adrenaline is contraindicated in the following pathological conditions; thyrotoxicosis, recent coronary occlusion, and uncontrolled hypertension. Nor should adrenaline, in any form, be administered to patients undergoing general anaesthesia using cyclopropane or halogenated hydrocarbon anaesthetics, because of the risk of producing cardiac arrhythmia. Adrenaline is also contraindicated for patients taking monoamine oxidase inhibitor drugs and in those who have used long-acting sympathomimetic drugs (e.g. as bronchodilators) within the preceding four hours. Dentally administered adrenaline is not contraindicated

for patients suffering from cardiovascular disease provided it is deposited extravascularly. Premedication of selected cases and careful use of local anaesthetic preparations containing adrenaline, assists in keeping the level of circulatory endogenous adrenaline to a minimum and avoiding side effects from this source.

Hypersensitivity and allergy to local anaesthetic agents, though uncommon, produce sufficiently serious systemic effects to merit routine pre-anaesthetic evaluation of all patients. Size and physical condition are important factors influencing sensitivity to local anaesthetic drugs. The heart may be sensitized to the action of local anaesthetics by disease and extravascular injection is mandatory for these patients.

The best defence against allergic response is through the taking of a medical history which includes, previous anaesthetic experience, history of associated allergic disorders, or familial tendency to develop allergy.

The need for careful pre-anaesthetic evaluation of patients to determine the existence of pathological conditions and abnormalities, or associated drug regimens which may influence the toxicity of local anaesthetic solutions is emphasized.

In view of the intravenous potency of contemporary dental local anaesthetic preparations and the high incidence

of vascular injury often associated with their administration, the avoidance of intravascular injection by preliminary aspiration has been given precedence as the most significant factor limiting local anaesthetic toxicity.

The paper reviews the problem of local anaesthetic toxicity as it currently exists in dentistry and is concerned with the prevention of systemic disturbances rather than their treatment. Accordingly, some original investigations were carried out with the object of expanding the available information on the controversial subject of intravascular injection.

A description has been presented of dissections of the pterygomandibular space and hard palate, illustrations of which accompany the text. The histology of these regions is also illustrated by photomicrographs of suitable prepared sections.

A more detailed aspiration survey than has previously been reported in the literature was devised to indicate not only the incidence but also the location of vascular injuries within the pterygomandibular space. The anatomy of this region had suggested a likely cause of the majority of vascular injuries associated with inferior alveolar nerve injection. The inferior alveolar vessels lie close to bone throughout their course in the mandibular sulcus and, since it is necessary to identify the floor of the sulcus by

contact during mandibular block, the vessels are sometimes caught between the needle point and bone, and punctured. This theory was confirmed by the aspiration survey which demonstrated also that 2-3 mm withdrawal from bone rarely failed to disengage vessels injured in this way.

Although the latter position is the accepted inferior alveolar nerve injection site, its significance in the avoidance of intravascular injection has been previously overlooked.

Notwithstanding the low incidence of vascular injury recorded at the inferior alveolar and lingual nerve injection sites, the quantity of local anaesthetic solution deposited at each of these positions, defines the need for routine pre-injection aspiration. It is also sound technique to reaspirate before injecting whenever the needle is moved within the tissues of the pterygomandibular space.

The anatomical and histological characteristics of the submucosal layer of the hard palate, suggest that intravascular injection in that region, is most likely to be associated with venepuncture occurring close to bone. As the needle approaches the larger, deeply placed vessels obtusely, they are sometimes caught between the point and underlying bone and punctured.

Since it is neither necessary nor desirable to contact bone during the greater palatine nerve injection, clinical

considerations prevent this claim being tested by an aspiration survey of the type used for mandibular injection.

However, it can be stated from the results of a short aspiration survey of infiltration injections and from recorded clinical observations that

(a) to minimize the incidence of vascular injury, the greater palatine and naso-palatine injection sites should be used for establishing palatal anaesthesia whenever possible.

(b) The greater palatine nerve injection should be given just in front of the greater palatine foramen and immediately beneath the lamina propria. The larger palatal vessels which lie close to bone in the submucosal layer are thereby avoided. This concept of a third dimension in needle placement is useful in reducing the incidence of injury to the palatal vasculature.

(c) Infiltration of local anaesthetic on the palatal aspects of the premolar teeth is contraindicated. The incidence of vascular injury here is higher because the main palatal vessels are enclosed in a thin submucosal layer between the lamina propria and periosteum. It is therefore more difficult to avoid the larger vessels in this position than at the greater palatine injection site where the submucosa has more depth.

(d) For the same reason, the choice of technique for establishing palatal anaesthesia adjacent to the canine tooth should be a matter for careful consideration. Dual nerve block may sometimes be preferable to local infiltration.

(e) Whether preliminary aspiration is observed or not, the palatal injection site should be closely watched for signs of intravascular injection while local anaesthetic is being slowly deposited.

Since the most frequent cause of increased systemic toxicity in dental local anaesthesia is intravascular injection, the main purpose of these investigations has been to consider ways of avoiding this undesirable complication. To this end, several recommendations have been made which contribute to better local anaesthetic technique.

BIBLIOGRAPHY

- ABRAHAMSON, D.I. BLOOD VESSELS AND LYMPHATICS,
1st Ed. New York, Academic Press Inc., 1962.
- ACCEPTED DENTAL REMEDIES,
13th Ed. Chicago, American Dental Association, 1961.
- ADRIANI, J. The clinical pharmacology of local
anesthetics.
J. Clin. Pharmacol. and Therap., 1: 645-673, 1960.
- ADRIANI, J. and Campbell, D. Fatalities following
topical application of local anesthetics to mucous
membranes.
J.A.M.A., 162: 1527-1530, 1956.
- ADRIANI, J. and Zepernick, R. Clinical effectiveness
of drugs used for topical anesthesia.
J.A.M.A., 188: 711-716 (May) 1964.
- AMERICAN DENTAL ASSOCIATION and AMERICAN HEART ASSOCIATION.
Management of dental problems in patients with cardio-
vascular disease.
J.A.D.A., 68: 333-342 (Mar.) 1964.
- AMERICAN MEDICAL ASSOCIATION. NEW DRUGS EVALUATED BY
the AMERICAN MEDICAL ASSOCIATION COUNCIL on DRUGS,
Chicago, American Medical Association, pp.143-155, 1966.
- ANON. Fatality from lignocaine.
Brit. M.J., p. 280 (Feb.) 1952.

ANWANDTER, G. The paralysis of the facial nerve after mandibular anesthetic injection.

Am. J. Orthodont. and Oral Surg., 30: (Dec.) 1944.

ARIENS, E.J. Pharmacology of catecholamines and their derivatives.

Arznumittel Forschung., 13: 541, 1963.

ASTROM, A. Recent advances in local analgesia.

Proc. roy. Soc. Med., 58: 415, 1965.

ASTROM, A. Pharmacological action of local anaesthetics.

Acta anaesth. scand., 25: 19-22, 1966.

ASTROM, A. and Persson, N.H. Some pharmacological properties of O-methyl-alpha-propylamino-propionanilide, a new local anaesthetic.

Brit. J. Pharmacol., 16: 32-44, 1961.

BARCROFT, H. Post haemorrhagic fainting. Study of cardiac output and forearm flow.

Lancet, 487, 1944.

BECKETT, A.H., Boyes, R.N. and Parker, J.B.R. Determination of lignocaine in blood and urine in human subjects undergoing local analgesic procedures.

Anaesthesia, 20: 3, 294-298 (July) 1965.

BELL, W.H. Emergencies in and out of the dental office: a pilot study in the State of Texas.

J.A.D.A., 74: 4, 778-783 (Mar.) 1967.

BERLING, C. Octapressin as a vasoconstrictor in dental plexus anaesthesia.

Odont. Rev., 17: 4, 369-385, 1966.

BERNS, J.M. and Sadove, M.S. Mandibular block injection: a method of study using an injected radiopaque material.

J.A.D.A., 65: 6, 735-745 (Dec.) 1962.

BISHOP, J.G., Dorman, H.L. and Matthews, J.L. Vasoconstrictors in local anaesthetics.

D. Clin. N. America, pp. 279-288 (July) 1961.

BJORN, H. LOCAL ANALGESIA and LOCAL ANALGESICS.

Sodertalje, Sweden, 1966.

BLACK, R.B. Aspirating gas-actuated syringe.

J.A.D.A., 74: 975 (April) 1967.

BLAXTER, P.L. and Britten, M.J.A. Transient amaurosis after mandibular nerve block.

Brit. med. J., 1: 681 (Mar.) 1967.

BOURNE, J.G. Fainting and cerebral damage: a danger in patients kept upright during dental anaesthesia and surgical operations.

Lancet, 2: 499, 1957.

BRAID, D.P. and Scott, D.B. Effect of adrenaline on the systemic absorption of local anaesthetic drugs.

Proc. I Second European Congress of Anaesthesiology,

Copenhagen 1966, pp. 334-346.

BRIERLEY, J.B. and Miller, A.A. Fatal brain damage after dental anaesthesia.

Lancet, 2: 869-873 (Oct.) 1966.

BROADBENT, B.G. Local anaesthetics - New solutions; Old fallacies.

D.J. Australia, 27: 5, 194-199 (Oct.) 1955.

BROADBENT, B.G. Primacaine hydrochloride - a new local anaesthetic agent.

Austral. D.J., 2: 2, 67-69 (April) 1957.

BROWN, G. Prilocaine - Felypressin dental anaesthesia (a preliminary study).

J. Oral Therap. and Pharmacol., 4: 6, 439-442, 1968.

BRUN, A. Effect of procaine, Carbocaine and lidocaine on cutaneous muscle in rabbits and mice.

Acta anaesth. scand., 3: 59, 1959.

BURCH, G.E. and De Pasquale, N.P. Arterial hypertension and the dental patient.

J.A.D.A., 73: 102-106 (July) 1966.

CAMPBELL, D. and Adriani, J. Absorption of local anaesthetics.

J.A.M.A., 168: 873-877 (Oct.) 1958.

CHERASKIN, E. and Prasertsuntarasai, T. Use of epinephrine with local anesthesia in hypertensive patients. I. Blood pressure and pulse rate observations in the waiting room.

J.A.D.A., 55: 761-774 (Dec.) 1957.

CHERASKIN, E. and Prasertsuntarasai, T. Use of epinephrine with local anesthesia in hypertensive patients. II. Effect of sedation on blood pressure and pulse rate in the waiting room.

J.A.D.A., 56: 2, 210-218 (Feb.) 1958 A.

Use of epinephrine with local anesthesia in hypertensive patients. III. Effect of epinephrine on blood pressure and pulse rate.

J.A.D.A., 57: 4, 507-519 (Oct.) 1958B.

CHERASKIN, E. and Prasertsuntarasai, T. Use of epinephrine with local anesthesia in hypertensive patients. IV. Effect of tooth extraction on blood pressure and pulse rate.

J.A.D.A., 58: 1, 61-68 (Jan.) 1959.

CHRISTENSEN, G. Preoperative medication for oral surgery patients.

Austral. D.J., 8: 5, 476-481 (Oct.) 1967.

CORBETT, T.R. and Helmore, F.E. Anaesthesia of the maxillary nerve via the greater palatine foramen.

Austral. D. Cong. (11th) Proc. p.137-145, 1948.

COSTICH, E.R. Reaction of rat muscle to the constituents of procaine epinephrine solutions in concentrations used for dental preparations.

Oral Surg., Oral Med. and Oral Path., 9: 205-210 (Feb.) 1956.

COSTICH, E.R. Study of inferior alveolar nerve block anaesthesia in humans comparing 2% procaine with 2% procaine plus 1:50,000 epinephrine.

J. D. Res., 35: 696-703 (Oct.) 1956.

COVENTRY, C.D. Intraosseous analgesia technique.

Austral. D.J., 2: 1, 36-37 (Feb.) 1957.

COWAN, A. Minimum dosage local anaesthesia.

Irish Jour. of Med. Science, 365-368 (Aug.) 1959.

CRAWFORD, J.S. Speculation: The significance of varying the mode of injection of a drug.

Brit. J. Anaesth., 38: 628-640, 1966.

CRISP, L.H. Reaction to procaine hydrochloride.

J.A.D.A., 47: 149 (Aug.) 1953.

CROUT, R.J. Sampling and analysis of catecholamines and metabolites.

Anesthesiology, 29: 4, 661-669, 1968.

CUNNINGHAM, D.J. TEXT-BOOK OF ANATOMY.

9th Ed. London, Oxford Univ. Press, 1953.

CUNNINGHAM'S MANUAL OF PRACTICAL ANATOMY. VOL. I.

12th Ed. London, Oxford Univ. Press.

DE JONG, R.H. and Walts, L.F. Lidocaine induced psychomotor seizures in man.

Proc. I Second European Congress of Anaesthesiology,

Copenhagen 1966, pp.598-604.

- DHUNER, K.G., Harthou, J.G.L., Herbring, B.G. and Lie, T.
Blood levels of mepivacaine after regional anaesthesia.
Brit. J. Anaesth., 37: 746 (Oct.) 1965.
- DHUNER, K.G. and Lewis, D.H. Effect of local anaesthetics
and vasoconstrictors upon regional blood flow.
Proc. I Second European Congress of Anaesthesiology,
Copenhagen 1966, pp.347-352.
- DICK, S.P. Clinical toxicity of epinephrine anesthesia.
Oral Surg., Oral Med. and Oral Path., 6:724-728 (June) 1953.
- DI GIOVANNI, A.J. Xylocaine convulsions: analysis of two
cases, intoxication or sensitization.
Anesth. and Analg., 42: 3, 355-359, 1963.
- DILLE, J.M. DRUG THERAPY FOR DENTISTS.
Chicago, Year Book Medical Publishers Inc., 1963.
- DOBBS, E.C. and Kader, M.I. Local anesthetic solutions;
their toxicity and treatment.
Oral Surg., Oral Med. and Oral Path., 3: 52-57 (Jan.) 1950.
- DOBBS, E.C. and Ross, N. The new local anesthetic,
Carbocaine.
New York State D.J., 27: 9, 453-457 (Nov.) 1961.
- DOUGLAS, B.L. Pain control in dental practice.
J. Tenn. S. Dent. Assn., 45: 3, 311-317, 1965.
- DUBIN, N.L. and Foner, L.M. Xylocaine. A report of 3000
clinical cases.
Oral Surg., Oral Med. and Oral Path., 5: 403-407 (Apr.) 1952.

ECCLES, J. The synapse.

Scien. Am., 212: 1, 56-66 (Jan.) 1965.

ELIS, J., Mattie, H., Laurence, D.R. and Prichard, B.N.C.
Modification by monoamine oxidase inhibitors of the effect
of some sympathomimetics on blood pressure.

Brit. med. J., 2: 75-78 (April) 1967.

ELLIS, H. and McLarty, M. ANATOMY FOR ANAESTHETISTS.

1st Ed. Oxford, Blackwell Scientific Publications, 1963.

ENGLESSON, S., Eriksson, E., Wahlqvist, S. and Ortengren, B.
Differences in tolerance to intravenous Xylocaine and
Citanest (L67), a new local anaesthetic. A double blind
study in man.

Proc. 1st Europ. Congress Anaesth. Vienna, II, 506, 1962.

ENGLESSON, S., Eriksson, E., Ortengren, B. and Wahlqvist, S.
Differences in tolerance to intravenous Xylocaine and
Citanest.

Acta anaesth. scand., Supplementum XVI, 141-145, 1965.

EPSTEIN, S. Local anesthetics: their characteristics and
use.

D. Clin. N. America, 37-56 (Mar.) 1958.

EPSTEIN, S. Clinical comparison of a new local anesthetic,
propitocaine, with lidocaine.

J. Oral Therap., 2: 3, 161-170 (Nov.) 1965.

- EPSTEIN, S. and Chilton, N. The clinical effectiveness of certain local anesthetics in dental procedures. Oral Surg., Oral Med. and Oral Path., 12: 1, 93-103 (Jan.) 1959.
- ERIKSSON, E., Granberg, P. and Ortengren, B. Study of renal excretion of Prilocaine and Lidocaine. Acta chir. scand., Suppl. 358: 55-69, 1966.
- ENRLICH, A. Administration of lidocaine and epinephrine (comment on epinephrine with local anaesthesia in hypertensive patients). J.A.D.A., 56: 428 (Mar.) 1958.
- EVERETT, F.G. A comparison of depth of anesthesia and toxicity of two and four percent procaine hydrochloride solution. J.D. Res., 28: 204-218 (June) 1949.
- FATHEREE, T.J. and Hines, E.A. Blood pressure responses to epinephrine administered intravenously to subjects with normal blood pressure and to patients with essential hypertension. Am. Heart J., 16: 66 (July) 1938.
- FEARON, R.W. AN INTRODUCTION TO BIOCHEMISTRY. 3rd Ed. London, William Heinemann, 1947.
- FISHER, S.J., Gehrig, J. and Green, H. Non-catechol amine vasopressor (PLV-2) as adjunct to local anesthesia. J.A.D.A., 70: 1189, 1965.

FOLDES, F.F. The influence of metabolic transformation on the toxicity of local anaesthetic agents in man. Proc. I Second European Congress of Anaesthesiology, Copenhagen, 1966, pp.591-597.

FOLDES, F.F., Molloy, R., McNall, P.G. and Koukal, L.R. Comparison of toxicity of intravenously given local anaesthetic agents in man. J.A.M.A., 172: 1493-1498, 1960.

FOLDES, F.F. and McNall, P.G. Toxicity of local anaesthetics in man. D. Clin. N. America, 257-278 (July) 1961.

FOLDES, F.F., Davidson, G.M., Duncalf, D. and Kuwabara, S. The intravenous toxicity of local anaesthetic agents in man. J. Clin. Pharmacol. and Therap., 6:3, 328-335 (May-June) 1965.

FORREST, J.O. Notes on aspiration before injection of local anaesthetics using dental cartridges. Brit. D.J., 107: 7, 259-262 (Nov.) 1959.

FOSTER, R.W. The pharmacology of pressor drugs. Brit. J. Anaesth., 38: 690-704 (Sept.) 1966.

FRYE, D.G. Aspirator syringes, facts and figures. J.A.D.A., 66: 145-146 (Jan.) 1963.

FULTON, G.P., Farber, E.M. and Moreci, A.P. The mechanism of action of rubefacients. J. Invest. Dermatol., 33: 317, 1958.

- GEDDES, I.C. Studies of the metabolism of Citanest Cl4.
Acta anaesth. scand., Supplementum XVI, 37-44, 1965.
- GLOVER, J. Vasoconstrictors in local anaesthetic solutions.
A general survey.
Austral. D.J., 58: 104-110 (Apr.) 1954.
- GLOVER, J. Short duration local anaesthetics.
The Mouth Mirror, 1963.
- GLOVER, J. Drug incompatibilities. Alupent.
Personal communication, 1967.
- GLOVER, J. Personal communication, 1967.
- GLOVER, J. Vasoconstrictors in dental anaesthetics. Contra-
indication - fact or fallacy?
Austral. D.J., 13: 1, 65-69 (Feb.) 1968.
- GOGERTY, J.H., Strand, H.A., Ogilvie, A.L. and Dille, J.M.
Vasopressor effects of topical epinephrine in certain dental
procedures.
Oral Surg., Oral Med. and Oral Path., 10:6, 614-622 (June)
1957.
- GOLDBERG, A. and Sadove, M. Further studies in the spread
of local anaesthetics.
J. Oral Surg., Anaes. and Hosp. D. Serv., 19: 232-236 (May)
1961.
- GOLDENBERG, M., Pines, K., Baldwin, E., Greene, D. and Roh, G.
The hemodynamic response of man to nor-epinephrine and
epinephrine and its relation to the problem of hypertension.
Am. J. Med., 5: 792-806 (Dec.) 1948.

GOLDMAN, V. Advances in local analgesia.
III Congressus Mundialis Anaesthesiologiae (Sept.) 1964,
pp. 320-334.

GOLDMAN, V. Citanest in dental surgery.
Acta anaesth. scand., Supplementum XVI, 297-311, 1965.

GOLDMAN, V. and Gray, W.A. A clinical trial of a new
local analgesic agent.

Brit. D.J., 115: 59-65 (July) 1963.

GOLDMAN, V., Killey, H.C. and Wright, H.C. Effects of
local analgesic agents and vasoconstrictors on rabbits'
ears.

Austral. D.J., 12:5, 460 (Oct.) 1967.

GOODMAN, L.S. and Gilman, A. THE PHARMACOLOGICAL BASIS
OF THERAPEUTICS.

3rd Ed. New York, The Macmillan Company 1966.

GORDH, T. Intravenous barbiturate anaesthesia in the
treatment of convulsions due to local anaesthetics.

Proceedings 2nd Congress Scand. Soc. Anaesth., Stockholm,
1952, pp. 67-69.

GORDH, T. Complications in connection with local
anaesthesia.

Acta anaesth. scand., Supplementum XVI, 137-139, 1965.

GORDON, R.A., Kerr, J.H. and Taylor, R. A laboratory
and clinical evaluation of mepivacaine (Carbocaine).

Canad. Anaesth. Soc. J., 7: 290 (July) 1960.

GRAUBARD, D.J., Robertuzzi, R.W. and Peterson, M.C.

Intravenous procaine: a preliminary report.

New York State J. Med., 47: 2187 (Oct.) 1947.

GRAY'S ANATOMY. DESCRIPTIVE AND APPLIED.

33rd Ed. Glasgow. The University Press, 1962.

GREENE, N.M. The metabolism of drugs employed in
anesthesia. Part II.

Anesthesiology, 29: 2, 327-360, 1968.

GRUBER, L.W. The relative efficiency of lidocaine and
mepivacaine as local anesthetics in dentistry.

New York J. Dent., 32: 7, 247-251 (Sept.) 1962.

GUYTON, A.C. Regulation of cardiac output.

Anesthesiology, 29: 2, 314-326, 1968.

HALL, R.K. Management of the sick and handicapped child
in general dental practice.

Austral. D.J., 12: 4, 323 (Aug.) 1967.

HARRIS, S.C. Adrenaline and analgesia.

J.D. Res., 26: 443, 1947.

HARRIS, S.C. Aspiration before injection of dental local
anesthetics.

J. Oral Surg., 15: 299-303 (Oct.) 1957.

HARRIS, S.C. Dental therapeutics, 1960.

J.A.D.A., 62: 502-510 (May) 1961.

HARRIS, S.C. Action of local anesthetic agents.

D. Clin. N. America, 231-241 (July) 1961.

HARRIS, S.C. and Worley, R.C. The relative local anaesthetic potencies of procaine, oracaine, kincaïne and xylocaine.

J.D. Res., 38: 477-482 (May-June) 1959.

HAYWARD, J.R. Complications in local anesthesia: prevention and treatment.

J. Oral Surg. Anaes. and Hosp. D. Serv., 19: 10-16 (Jan.) 1961.

HEINONEN, J. Influence of some drugs on toxicity and rate of metabolism of lidocaine and mepivacaine; experimental study on mice and rats.

Ann. Med. Exper. Biol. Fenn., 44: suppl. no. 3, 43, 1966.

HELMORE, F.E. Emergencies in dental practice - part II. Austral. D.J., 8: 5, 415-417 (Oct.) 1963.

HENN, F. Determination of the toxicological and pharmacological properties of Carbocaine, lidocaine and procaine by means of simultaneous experiments, a critical comparison.

Acta anaes. scand., 4: 3, 125, 1960.

HIATT, W. Local anesthesia: history; potential toxicity; clinical investigation of mepivacaine.

D. Clin. N. America, 243-256 (July) 1961.

HOFMEYR, C.F.B. Investigation into the toxicity of Carbocaine - a new local anaesthetic.

J. South African Vet. M.A., 30: 4, 459, 1959.

HOLROYD, S.V., Watts, D.T. and Welch, J.T. The use of epinephrine in local anaesthetics for dental patients with cardiovascular disease: a review of the literature. J. Oral Surg. Anaes. and Hosp. D. Serv., 18: 492-503 (Nov.) 1960.

HOLL, G. and Hood, F.J. An anaphylactoid reaction to lignocaine.

Dental Pract., 15: 294 (April) 1965.

HOWARD, P., Leathart, G.L., Dornhorst, A.C. and Sharpey-Schafer, E.P. The "Mess Trick" and the "Fainting Lark". Brit. med. J., 2: 382-384 (Aug.) 1951.

HUGHES, C.L., Leach, J.K., Allen, R.E. and Lambson, G.O. Cardiac arrhythmias during oral surgery with local anesthesia.

J.A.D.A., 73: 1095-1102 (Nov.) 1966.

JAMES, A.G. Weather conditions affecting patients' reaction to local anaesthetics. III. A report of 1,103 consecutive cases using lidocaine.

J.D. Res., 34: 268-272 (Apr.) 1955.

JAMIESON, E.B. A COMPANION TO MANUALS OF PRACTICAL ANATOMY.

7th Ed. London, Oxford University Press, 1962.

JENSEN, J. Adrenalin test in hypertension.

Am. Heart J., 5: 763 (Aug.) 1930.

- JOLLY, M. Pre-operative assessment of the dental patient.
Austral. D.J., 12: 3, 258-269 (June) 1967.
- KALOW, W. Pharmacogenetics and anesthesia.
Anesthesiology, 25: 377-387, 1964.
- KATZ, B. How cells communicate.
Scien. Am., 3-11 (Sept.) 1961.
- KATZ, R.L. Epinephrine and PLV-2: Cardiac rhythm and
local vasoconstrictor effects.
Anaesthesiology, 26: 619-623 (Sept.-Oct.) 1965.
- KAUFMAN, L. Arrhythmias linked to extractions.
Dental Times, 15th May 1966.
- KEMP, H.R. Local anaesthesia for general dental practice.
Queensland D.J., 5: 221-230 (Oct.-Nov.) 1953.
- KEMP, H.R. A few pertinent comments on the use of local
anaesthetic solutions.
Austral. D.J., 2: 5, 295-298 (Oct.) 1957.
- KEMP, H.R. Notes on local anaesthesia.
Dept. of Oral Surgery, Univ. Syd. (Aug.) 1965.
- KEMP, H.R. and Jolly, M. Local anaesthesia.
D. Mag. and Oral Topics, 79: 29-30 (Mar.) 1962.
D. Mag. and Oral Topics, 79: 148-150 (Sept.) 1962.
- KENNEDY, P.J. Local Analgesia.
M.D.S. Thesis Univ. Sydney 1965.

KENNEDY, W.F. jr., Bonica, J.J., Ward, R.J., Tolas, A.G.,
Martin, W.E. and Grinstein, A.

Cardiorespiratory effects of epinephrine when used in
regional anaesthesia.

Proc. I 2nd European Congress of Anaesthesiology,
Copenhagen, 1966, pp.320-333.

KIMMEY, J.R. and Steinhaus, J.E. Cardiovascular effects
of procaine and lidocaine during general anaesthesia.
Federation Proc. 17, 384, 1958.

KNOX, P.R., North, W.C. and Stephen, C.R. Pharmacologic
and clinical observations with mepivacaine.
Anaesthesiology, 22: 6, 987-994 (Nov.-Dec.) 1961.

KOBAYASHI, I. et al. Experimental study on the method
of block anaesthesia using an injected radiopaque material.
I. Mandibular block.

Oral Res, Abs., 3: 104 (Feb.) 1968.

KUTSCHER, A.H. and Mercadante, J. Local anaesthetics:
results of cooperative research survey III.
New York State D.J., 24: 210-214 (May) 1958.

LAVINE, M.H., Stoopack, J.C. and Jerrold, T.L. An
adrenal crisis secondary to extraction of a tooth in a
patient with panhypopituitarism.

J.A.D.A., 76: 2, 354-358 (Feb.) 1968.

- LAWRENCE, Van S., Marte, E., Brown, B. and Van Bergen, F.
Lidocaine, 2-chlorprocaine and hepatic necrosis.
Anesth. and Analg., 45: 1, 55-58 (Jan-Feb.) 1966.
- LAZANSKY, J.P. and Robinson, L. Study of the effectiveness
of Xylocaine as a local anaesthetic agent in dentistry.
Oral Surg., Oral Med. and Oral Path., 2: 1286-1297 (Oct.)
1949.
- LE CHAT, P. and Deleau, D. Pharmacological study of a
new local anaesthetic, mepivacaine (Carbocaine).
Anesth. et Analg., 18: 78 (Jan.-Mar.) 1961.
- LIGHT, G.A. A new vasoconstrictor - Preliminary studies
with Phenylpressin.
Anaes. and Analg., 44: 280, 1965.
- LINDSAY, B. Applied anatomy in local anaesthesia.
Austral. J. Dent., 52: 110-113 (Mar.) 1948.
- LIVINGSTON, W.K. What is pain?
Scien. Am., (Mar.) 1953.
- LOCKE, R.S. Local anaesthesia: its uses and abuses.
P.D.M., 5-31 (May) 1961.
- LOOBY, J.P. and Kirby, C.K. Use of hyaluronidase with
local anaesthetic agents in dentistry.
J.A.D.A., 38: 1-4 (Jan.) 1949.
- LUDUENA, F.P. Local effects of various drugs on the
duration of infiltration anaesthesia produced by dental
anaesthetic solutions.
J. D. Res., 36: 613-622 (Aug.) 1957.

- LUDUENA, F.P. The pharmacology and toxicology of mepivacaine, a new local anaesthetic.
Toxicol. and Appl. Pharmacol., 2: 295 (May) 1960.
- LUDUENA, F.P., Ananenko, E., Siegmund, O.H. and Miller, L.C. Comparative pharmacology of the optical isomers of arterenol.
J. Pharmacol. Exper. Therap. 95: 155-170, 1949.
- LUDUENA, F.P. and Hoppe, J.O. 2 Alkoxy benzoate and thiolbenzoate derivatives as local anesthetics.
J. Pharmacol. and Exper. Therap. 117: 39, 1956.
- LUNDQVIST, B., Lofgren, N., Persson, H. and Sjogren, B. Metal ions as a cause of swelling after local anaesthesia in dental practice.
Acta Chir. Scand., 97: 3, 239-258, 1948.
- LUNDY, G.J. What the dentist should know about angina pectoris, coronary thrombosis and arteriosclerosis.
D. Digest, 45: 104 (Mar.) 1939.
- LUTZKI, A. von. Citanest - a new local anaesthetic. Pharmacology and clinical investigations - a review.
Astra, 1964.
- MAHER, W.P. and Swindle, P.F. Submucosal blood vessels of the palate.
D. Progress, 2: 167-180 (Apr.) 1962.
- MARTIN, W.E., Kennedy, W.F. jr., Bonica, J.J., Stegall, F. and Ward, R.J. Effect of epinephrine on arteriolar vasodilation produced by brachial plexus block.
Proc. I Second European Congress of Anaesthesiology, Copenhagen 1966, pp.313-319 Acta anaes. scand.

MATTHERS, H. and Schabert, P. Mepivacain blood level after injection into various tissues.

Anaesthetist, 15: 59 (Feb.) 1966.

MATTHEWS, J.L., Bishop, J.G., Moore, E.E. and Dorman, H.L. Blood flow and blood pressure responses to mandibular nerve blocking agents.

J.D. Res., 38: 276-288 (Apr.) 1959.

MCCARTHY, F.M. Clinical study of blood pressure responses to epinephrine-containing local anesthetic solutions.

J.D. Res., 36: 1, 132-141 (Feb.) 1957.

MCCHESENEY, E.W., McAuliff, J.P. and Blumberg, H. The hyperglycaemic action of some analogs of epinephrine.

Proc. Soc. Exp. Biol. Med., 71: 220, 1949.

MELLUSI, J. Differential diagnosis of syncope.

Anesth. Progr., 4-11 (Jan.) 1967.

MELZACK, R. The perception of pain.

Scien. Am., 204 (Feb.) 1961.

MERCURIO, J.P. Emergency submental injection.

J.A.D.A., 74: 717-719 (Mar.) 1967.

MITCHELL, H.S. Allergy to local anaesthetic agents.

J. Can. Dental Assoc., 19: 127, 1953.

MONHEIM, L.M. LOCAL ANAESTHESIA AND PAIN CONTROL IN DENTAL PRACTICE.

3rd Ed. St. Louis, C.V. Mosby Co., 1965.

MOORE, D.C. **COMPLICATIONS OF REGIONAL ANESTHESIA.**

1st Ed. Oxford, Blackwell Scientific Publications, 1955.

MOORE, D.C. and Green, J. **Toxic reactions to local anaesthetics.**

D. Abs., 2: 135 (Mar.) 1957.

MOORE, D.C. and Bridenbaugh, L.D. **Oxygen: the antidote for systemic toxic reactions from local anaesthetic drugs.**

D. Abs., 6: 276 (May) 1961.

MORRIS, A.L. **The medical history in dental practice.**

J.A.D.A., 74: 1, 129-137 (Jan.) 1967.

MORRISET, L.M. **Fatal anaphylactic reaction to lidocaine.**

D. Abs., 2: 686 (Nov.) 1957.

MUMFORD, J.M. and Geddes, I.C. **Adrenaline, its role in local anaesthetic solutions for dentistry.**

D. Practitioner and D. Record, 10: 2-5 (Sept.) 1959.

MUMFORD, J.M. and Geddes, I.C. **Trial of Carbocaine in conservative dentistry.**

Brit. D.J., 110: 92-94 (Feb.) 1961.

MYERS, H.M. **Pharmacology and therapeutics - local anaesthetics.**

J.A.D.A., 74: 1488-1490 (June) 1967.

NEVIN, H.R. **Toxicity following mandibular injection and nose bleed following posterior palatine injection.**

D. Items. Interest, 74: 452-453 (May) 1952.

NEVIN, M. PROBLEMS IN DENTAL LOCAL ANESTHESIA.

1st Ed. New York, Dental Items of Interest Publishing Co. Inc., 1952.

NEVIN and PUTERBAUGH. CONDUCTION, INFILTRATION and GENERAL ANESTHESIA in DENTISTRY.

London, Dental Items of Interest Publishing Co. Inc., 1938.

NEW YORK HEART ASSOCIATION. Report of the special committee of the New York Heart Association Inc. on the use of epinephrine in connection with procaine in dental procedures. J.A.D.A., 52: 108 (Jan.) 1955.

NEWMAN, C.W. and Holt, R.T. Use of aspirating syringes for local anaesthesia.

J.A.D.A., 72: 1119-1121 (May) 1966.

NINGHAM, L.R. and Malherbe, P.H. Xylocaine intoxication: a report of three cases.

D. abs., 3: 143 (Mar.) 1958.

NOBLE, D.W. and Pierce, C.F. Allergy to lignocaine. A case history.

Lancet, 2: 1436 (Dec.) 1961.

NORDENRAM, A. Local anaesthesia with Carbocaine in dentistry in the light of new investigations.

Odont. Foren. T., 25: 359 (Dec.) 1961.

ONJI, Y. and Tyuma, I. Methemoglobin formation by a local anesthetic and some related compounds.

Acta anaesth. scand., Supplementum XVI, 151-159, 1965.

ORBANS ORAL HISTOLOGY AND EMERVOLOGY.

St. Louis, The C.V. Mosby Co., 1966.

ORINJER, M.J. Roles of minimal dosage and vasoconstriction in safety and efficiency of local anaesthesia: physiological effects and technique of administration.

Oral Surg., Oral Med. and Oral Path., 2: 1566-1574 (Dec.) 1949.

PATON, U.D.M. The principles of drug action.

Proc. roy. Soc. Med., 53: 815 (Mar.) 1960.

PICKERING, G.W. and Kissin, M. Effects of adrenaline and of cold on the blood pressure in human hypertension.

Clin. Sc., 2: 201 (May) 1936.

PRESCRIPTION PROPRIETARIES GUIDE.

5th Ed. Melbourne, Australian Pharmaceutical Publishing Co. Ltd., 1968.

RAND, M.J. and Trinker, F.R. Pharmacological agents affecting the release and activity of catecholamines.

Brit. J. Anaesth., 38: 666-689 (Sept.) 1966.

ROBSON, J.M. and STACEY, R.S. RECENT ADVANCES IN PHARMACOLOGY.

3rd Ed. London, J. and A. Churchill Ltd., 1962.

SACHS, J.S. Present status of procaine toxicity.

J. Oral Surg., 7: 312-314 (Oct.) 1949.

SADOVE, M.S. Clinical experience with Citanest; a new local anesthetic.

Acta anaes. scand. Supplementum XVI, 271-276, 1965.

SADOVE, M.S. and Kolodny, S.G. Local anaesthetic agents in combination with vasoconstrictors. Part I. Adrenaline. Acta anaesth. scand. 5: 13, No. I, 1961.

SADOVE, M.S. Classification and management of reactions to local anesthetic agents.

J.A.M.A., 148: 17-22 (Jan.) 1952.

SADOVE, M.S. An evaluation of mepivacaine hydrochloride. J. Oral Surg., Anaes. and Hosp. D. Serv., 20: 398-404 (Sept.) 1962.

SALMAN, I. and Schwartz, S.P. Effects of vasoconstrictors used in local anaesthetics in patients with diseases of the heart.

J. Oral Surg., 13: 209-213 (July) 1955.

SARA, C. Emergencies in dental practice. Part I. Austral. D.J., 8: 5, 408-414 (Oct.) 1963.

SARA, C. Post-Graduate lecture notes (May) 1967.

SARA, C. Personal communication, (July) 1968.

SCANDINAVIAN PHARMACOPOEIA COUNCIL.

Monograph A 56/57, (July) 1957.

SGHIANO, A.M. and Strambi, R.G. Frequency of accidental intravascular injection of local anaesthetics in dental practice.

Oral Surg., Oral Med. and Oral Path., 17: 178-184 (Feb.) 1964.

SCHIRGER, A., Waite, D.E. and Martin, W.J. Some medical aspects of the dental patient.

J.A.D.A. 75: 6, 1379-1384 (Dec.) 1967.

SELDIN, H.M. and Recant, B.S. The safety of anesthesia in the dental office.

J. Oral Surg., 13: 199-208 (July) 1955.

SELDIN, H.M. Survey of anaesthetic fatalities in oral surgery and a review of the etiological factors in anaesthetic deaths.

D. abs., 3: 423-424 (July) 1958.

SCOTT, D.B. Plasma levels of local analgesic in man following epidural and intercostal nerve block.

III Congressus Mundialis Anaesthesiologiae, (Sept.) 1964.

SHANNON, I.L., Prigmore, J.R. and Isbell, G.M. Stress patterns in dental patients: the adrenocortical response to a scheduled appointment for exodontia.

J.D. Res., 40: 758 (July-Aug.) 1961A.

SHANNON, I.L., Prigmore, J.R. and Isbell, G.M. Stress patterns in dental patients: I serum free 17 hydroxycorticosteroids, sodium and potassium in subjects undergoing local anaesthesia and simple exodontic procedures.

J. Oral Surg., Anaes. and Hosp. D. Serv., 19: 486-491 (Nov.) 1961B.

SHARPEY-SCHAFFER, E.P. Syncope.

Brit. med. J., 1: 506-509 (Mar.) 1956.

SHARPEY-SCHAFFER, E.P., Hayter, C.J. and Barlow, E.D.

Mechanism of acute hypotension from fear or nausea.

Brit. med. J., 2: 878-880 (Oct.) 1958.

SHEPHERD, R.W. Prosthetic treatment for the older patient.

Austral. D.J., 12: 4, 339 (Aug.) 1967.

SHIP, I.I. Response of systolic and diastolic blood pressures to dental stress.

Oral Surg., Oral Med. and Oral Path., 13: 499-507 (Apr.) 1960.

SHIRA, R.B. New injection technics.

D. Abs., 8: 118 (Feb.) 1963.

SHOTWELL, J.E. Toxic effects following the use of local anaesthetic agents.

Oral Surg., Oral Med. and Oral Path., 1: 730-734 (Aug.) 1948.

SICHER, H. The anatomy of mandibular anesthesia.

J.A.D.A., 33: 1541-1557 (Dec.) 1946.

SICHER, H. ORAL ANATOMY.

4th Ed. St. Louis, The C.V. Mosby Company, 1965.

SLOTNICK, I.L. and Teigland, J.D. Cardiac accidents following vasopressin injection (Pitressin).

J. Am. Med. Ass., 146: 1126-1128 (July) 1951.

SMITH, N. An investigation of the influence of gauge on some physical properties of hypodermic needles. Part I & II.

Austral. D.J., 13:2, 158-161 (Apr.) 1968A.

Austral. D.J., 13:2, 161-163 (Apr.) 1968B.

SMITH, C.J. and Cimasoni, G. Cholinesterases in buccal and gingival mucosa of monkey and man. Histochemical demonstration and effect of local anaesthetics.

Arch. Oral Biol. 12:3, 349-354 (Mar.) 1967.

SPIRO, S.R. Common errors resulting in inadequate regional analgesia and management of complications.

New York J. Den., 36: 159-162 (May) 1966.

STEINHAUS, J.E. A comparative study of the experimental toxicity of local anesthetic agents.

Anaesthesiology, 13: 577-586 (Nov.) 1952.

STEINHAUS, J.E. Local anesthetic toxicity: a pharmacological re-evaluation.

Anaesthesiology, 18: 275-281, 1957.

STEINHAUS, J.E. Toxic reactions to local anesthetics.

The Journal of the Medical Assoc. of the State of Alabama, 32: 6, 168-172 (Dec.) 1962.

SWEETS, R.B. Anaphylactic shock after local anaesthetic.

D. Abs., 8: 117-118 (Feb.) 1963.

TAINTER, M.L. and Thronson, A.H. Influence of vasoconstrictors on the toxicity of procaine anesthetic solutions.

J.A.D.A., 25: 966-979 (June) 1938.

TAINTER, M.L., Thronson, A.H. and Moose, S.M. Vasoconstrictors on the clinical effectiveness and toxicity of procaine anesthetic solutions.

J.A.D.A. and D. Cosmos, 25: 1321-1334 (Aug.) 1938.

TAINIER, M.L. and Winter, L. Some general considerations in evaluating local anaesthetic solutions in patients. *Anaesthesiology*, 5: 470-490 (Sept.) 1944.

TAINIER, M.L., Luduena, F.P. and Hoppe, J.O. The trend to more potent local anaesthetic solutions in dentistry. *Oral Surg., Oral Med. and Oral Path.*, 6: 645-661 (May) 1953.

TILLMAN, H.H. Problems of allergy encountered in dentistry. *Oral Surg., Oral Med. and Oral Path.*, 11: 1372-1377 (Dec.) 1958.

TOLAS, A.G., Allen, G.D., Ward, R.J., Kennedy, W.F. jr. and Bonica, J.J. Comparison of effects of methods of induction of anesthesia on cardiac rhythm. *J. Oral Surg.* 25: 1, 54-59 (Jan.) 1967.

TOOGOOD, J.H. Reactions to local anaesthetics. *J. Can. Dental Assoc.* 26: 4 (April) 1960.

TRINKER, F., Fearn, H.J., McCulloch, M.W. and Rand, M.J. Experimental observations on the effects of adrenaline after treatment with antidepressant monoamine oxidase inhibitor (MAOI) drugs.

Austral. D.J., 12: 4, 297-303 (Aug.) 1967.

TRUANT, A.P. Local anaesthetic and toxicologic properties of Citanest.

Acta anaesth. scand. Supplementum XVI, 19-22, 1965.

TRUANT, A.P. and Wiedling, S. A contribution to the pharmacological and toxicological evaluation of a new local anaesthetic, d, l, N-methylpipercolyl-2, 6 xylydide. Acta chir. scand., 116: 351 (May) 1959.

ULFENDAHL, H.R. Some pharmacological and toxicological properties of a new local anaesthetic, Carbocaine. Acta anaesth. scand., 1: 81 (Dec.) 1957.

VALLINI, R. and Gaiatto, S. Pharmacological researches concerning a new local anaesthetic named Citanest. Annals of the University of Ferrara, Section XI - Pharmacology and Therapy, 11: 9, 101, 1963.

VERNALE, C.A. Cardiovascular responses to local anaesthesia with epinephrine in normotensive and hypertensive subjects.

Oral Surg., Oral Med. and Oral Path., 13: 942-952 (Aug.) 1960.

WALDMAN, H.B. and Binkley G. Lidocaine hypersensitivity: report of case.

J.A.D.A., 74: 747-749 (Mar.) 1967.

WALLACE, D.A., Sadove, M.S., Spence, J.M. and Gish, G. Systemic effects of dental local anaesthetic solutions. Oral Surg., Oral Med. and Oral Path., 9: 1297-1303 (Dec.) 1956.

- WALTERS, J.D. Toxicity of local anaesthetics.
J.A.D.A., 31: 94-101 (Jan.) 1950.
- WATERSON, J.G. Anaesthesia as a dental problem.
Austral. D.J., 12: 4, 343-347 (Aug.) 1967.
- WEIL, C., Welham, F.S. and Yackel, R.F. Clinical
evaluation of mepivocaine hydrochloride by a new method.
J.A.D.A., 63: 26-32 (July) 1961.
- WIEDLING, G. Effect of local anaesthetics in combination
with vasoconstrictors on blood pressure.
Austral. J. Dent., 53: 180-184 (June) 1954.
- WIEDLING, S. Studies on alpha-n-propylamino-2-
methylpropionanilide, a new local anaesthetic.
Acta Pharmacol. et Toxicol., 17: 233-244, 1960.
- WIEDLING, S. XYLOCAINE. THE PHARMACOLOGICAL BASIS OF
ITS CLINICAL USE.
2nd Ed. Stockholm, Almqvist and Wiksell, 1964.
- WIEDLING, S. and TEGNER, G. PROGRESS IN MEDICINAL CHEMISTRY.
LOCAL ANAESTHETICS.
London, Butterworths, 1963.
- WEGAND, F.T. Untoward reaction to lidocaine: report of
a case.
J. Oral Surg., 16: 334-336 (July) 1958.
- WILLIAMS, R.M., Koyes, H., Becker, D.J., Williams, R.A. and
Wasserman, F. Electrocardiographic changes during oral
surgical procedures under local anesthesia.
Oral Surg., Oral Med. and Oral Path., 16: 10, 1270-1275
(Oct.) 1963.

WITTROCK, J. and Fischer, W. The aspiration of blood
through small gauge needles.

J.A.D.A., 76: 1, 79-81 (Jan.) 1968.

WOLCOTT, M.W. Cardiac resuscitation.

The Journal of The American Dental Society of Anesthesiology.

10: 34-40 (Feb.) 1963.

WOOD-SMITH, F.G. and Stewart, H.C. DRUGS IN ANAESTHETIC
PRACTICE.

London, Butterworths, 1963.

XYLOCAINE.

Brit. med. J., 1: 211 (Jan.) 1952.