BRACHIAL PLEXUS BLOCKADE BY LIDOCAINE ONE PERCENT WITH ADRENALINE 1:200,000 FOR UPPER LIMB SURGERY "A PRELIMINARY LITERATURE REVIEW AND CLINICAL EXPERIENCE"

BY

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Brachial Plexus Blockade By Lidocaine one Percent with Adrenaline 1:200,000 For Upper Limb Surgery. "A Preliminary Literature Review And Clinical Experience"

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CERTIFICATE

I certify that this dissertation was the result of my personal effort. Help and guidance in conducting the study was offerred by members of staff of the Department of Anaesthesiology of the University of Dar es Salaam.

DECLARATION

I hereby declare that, this dissertation either in part or in whole has not been submitted for a degree in any other University.

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SUMMARY:

Brachial plexus blockade anaesthesia for upper limb surgery was performed using lidocaine 1% with adrenaline 1:200,000 solution. The random study population consisted of 40 patients. Two approaches of achieving brachial plexus blockade were studied and compared. Twenty patients were blocked by each of the two approaches. There was an overall success rate of 87.5%. The blockade success rates were 90% and 85% by the axillary and supraclavicular routes respectively. These success rates are similar to those reported by other studies. There was a 15% incidence of complications by the supraclavicular route, while it was 5% in the axillary group. These results compare well with other studies which also report a higher incidence of complications associated with the supraclavicular approach than the axillary approach.

The mean onset of analgesia in the supraclavicular and axillary group was 13.99 $\pm$ 2.49 and 14.92 $\pm$ 2.59 minutes respectively. There was no significant difference in the mean duration of analgesia in the two approaches. These results are similar to those reported from various other studies.

INTRODUCTION

Trauma accounts for many upper limb surgical operations. Most of these cases present to the anaesthesiologist as emergencies and anaesthesia will thus be conducted in a patient without adequate prior preparation. In such situations general anaesthesia is associated with several risks. Regurgitation and aspiration of gastric contents is an ever present risk. Patients who are debilitated or in shock might not fair well with general anaesthesia. Cardiopulmonary disorders are frequently encountered in such unprepared surgical emergencies and these pose a major risk particularly in the older age groups. A method of regional anaesthesia on the upper limb would thus circumvent all the would be risks for general anaesthesia.

With regional anaesthesia, the patient remains awake, retains his protective reflexes and breathes without respiratory depression secondary to general anaesthetics. The patient benefits from a prolonged post surgical analgesia without the need of parenteral narcotic analgesics. This effect is most pronounced with the newer longer acting local anaesthetic drugs like bupivacaine (marcaine) and etidocaine (Duranest). Moreover the patient enjoys a good postoperative period free from nausea, vomitting or cerebral depression and also provides early postoperative ambulation.

Brachial plexus blockade for upper limb surgery provides good operating conditions in that there is complete relaxation of the muscles of the upper extremity thus simplifying closed reduction of fractures and dislocations or the approximation of severed tendons. There is sympathetic

blockade of the blood vessels which lessens postoperative vasospasm, pain and oedema (de Jong 1961). Brachial plexus blockade like other regional anaesthetic techniques, causes less disturbance of body functions. The techniques prevent or reduce the endocrine-metabolic response to surgery and the postoperative nitrogen balance is improved (Kehlet 1982). Most of the upper limb operations can be done by brachial plexus blockade anaesthesia. The technique is simple and requires the minimum of equipment, drugs and patient monitoring. Moreover the method is cheaper than a general anaesthetic technique. The drugs used are nonvolatile and unlike inhalational general anaesthetics there is no pollution to the environment. There are also no risks of explosions since the drugs are non inflammable.

At Muhimbili Medical Centre most of the operations are done under general anaesthesia. Very few operations are done under regional anaesthesia and still a negligibly small number of upper limb operations are done by brachial plexus blockade. General anaesthesia management requires expensive and often complicated equipment and a close supervision by a trained anaesthesiologist is mandatory. In our setting, there are very few trained anaesthesiologists to cope up with the ever-increasing work load. In order to deal with this burden, one would resort to regional anaesthetic techniques wherever indicated. Brachial plexus blockade can be easily learned and done by any doctor and in so doing reduce the need of having an anaesthesiologist to give general anaesthesia. This will give time for the few available anaesthesiologists to cater for other more demanding operative procedures. The application of the technique at outpatient departments

and operating theatres would save the already meagre health budget both in terms of costs for general anaesthesia management and personell time. Moreover more safety is guaranteed for the patients. It was thus found appropriate to do a study on brachial plexus blockade for upper limb surgeries at the Muhimbili Medical Centre operating theatre.

The brachial plexus blockade study using lidocaine 1% with adrenaline solution was done in 40 patients who were randomly selected. Two approaches of brachial plexus blockade were used, the supraclavicular approach and the axillary approach. In each there were 20 patients. The overall brachial plexus blockade success rate was studied and the success rates by each of the two approaches was studied. The nature and incidence of complications was studied in each of the approaches used. The latency of analgesia and the duration of analgesia in each of the approaches were studied. Finally the two approaches were compared in terms of success rate, complications, latency (onset) of analgesia and duration of analgesia.

PART I

LITERATURE REVIEW ON BRACHIAL PLEXUS BLOCK

PART I: LITERATURE REVIEW ON BRACHIAL PLEXUS BLOCK

1 - 1 INTRODUCTION:

Brachial plexus block is the injection of a local anaesthetic agent into the brachial plexus for the production of regional analgesia of the upper limb which is innervated via the plexus.

Earlier techniques attempted to locate the plexus, whether via the supraclavicular or axillary routes, and to deposit anaesthetic solution at each of the several elements derived from the plexus. These techniques required multiple injections and hence carried an increased risk of complications. The more recent perivascular techniques utilize the concept that there is a fascial envelope surrounding the plexus throughout most of its course. Therefore, just as with peridural anaesthesia, brachial plexus anaesthesia can be produced by a single injection into this perineural space, and the extent of the anaesthesia which results will depend on the level of injection and the volume of anaesthetic injected (Collins 1976).

1 - 2 HISTORY OF BRACHIAL PLEXUS BLOCKADE

It was Halstead who in 1884 performed the first brachial plexus blockade by exposing nerve roots in the neck and then directly applying cocaine solution on them. In 1897 Crile of Cleveland was able to disarticulate the shoulder joint after exposing the brachial plexus above the clavicle and then injecting each trunk with

a 0.5 percent cocaine solution. In the same year Matas of New-Orleans was also able to block the brachial plexus at direct vision after dissection above the clavicle (Macintosh and Mushin 1954, Atkinson et al 1977).

Later in 1911, Hirschel a German Surgeon at Heidelberg injected the brachial plexus in the axilla blindly by using a percutaneous technique. He was thus the first to describe the axillary approach to brachial plexus blockade (Hirschel G 1911). In 1912, Kulenkampff a German Surgeon working at Zwickau used a 2% procaine solution to do a blind blockade of the brachial plexus through a Supraclavicular approach. He used no landmarks in his description and this consequently led to a high rate of blockade failures (Macintosh and Mushin 1954).

Several workers including Babitski in 1918, Bazy and Blondin 1935 Dogliotti in 1939 and Sherwood - Dunn 1920 attempted the infraclavicular route to the brachial plexus. The technique never became popular for adoption ;because of the unreliability of results, the likelihood of vascular damage and the increased risk of intravascular injection (Macintosh and Mushin 1954). Before 1940, methods of brachial plexus blockade had the disadvantage of uncertainity of success. This was due to lack of anatomical description and absence of landmarks. In 1940 Patrick a Surgeon at Glasgow modified the Kulenkampffs' techinique for the

supraclavicular blockade by giving it anatomical landmarks (Patric 1940). Patrick aimed at infiltrating the tissue between the midclavicular point on the skin and the first rib by starting the injections lateral to the plexus and working medially, until the subclavian artery pulsations transmitted along the needle indicated that the lower trunk of the plexus had been reached. (Atkinson et al 1977). In 1944 Macintosh and Mushin modified Patricks technique, by starting injections into the lower trunk close to the subclavian artery and then working laterally. Todays description of Kulenkampff's technique is the Macintosh and Mushin modification.

After Hirschel had done the first blind axillary brachial plexus blockade, Accardo and Adriani 1912, improved on the technique by injecting the terminal nerves of the plexus individually in the axilla where they are closely related to the axillary artery. Burnham 1958 described the proximity of the nerves of the plexus to the axillary artery and pointed out the presence of a perivascular space enclosed by a fascial sheath. He suggested injecting individual nerves within the neurovascular sheath. He thus for the first time introduced the axillary perivascular technique of brachial plexus blockade. Father 1958 supported Burnham and suggested that the pulsating axillary artery was the most important landmark in the axillary perivascular block of the plexus. De Jong 1961, stresses the importance of injecting a sufficient volume of anaesthetic solution into the neurovascular

sheath by multiple injections, in order to ensure blockade. Winnie and Collins showed by using radio-opaque dye injections, that the perivascular space was a continuous fascia-enclosed space extending from the cervical transverse processes to several centimeters beyond the axilla, after this discovery they described a subclavian perivascular technique utilizing a single injection and a large volume of anaesthetic solution (Winnie and Collins 1964). This technique was still supraclavicular and as such it carried with it the possible complications of subclavian artery puncture and pneumothorax.

Winnie 1970, improved on the subclavian perivascular technique and approached the brachial plexus sheath high up in the neck via the interscalene space opposite C_6. He thus introduced the Interscalene approach to the brachial plexus (Winnie Interscalene Brachial plexus Block).

More recently, Whiffler 1981, has reintroduced and modified the infraclavicular brachial plexus blockade by introducing the coracoid approach.

1 - 3 ANATOMICAL CONSIDERATIONS OF THE BRACHIAL PLEXUS

The brachial plexus is derived from the anterior primary divisions of five spinal nerves - C_5 C_6 C_7 C_8 and T_1. Communicating loops from C_4 and T_2 spinal nerves contribute to the plexus. The plexus forms the entire motor and almost all the sensory nerve

supply to the arm (Collins 1976). Sympathetic contributions enter the anterior primary spinal nerve and originate from the middle and inferior cervical sympathetic ganglia in the form of gray rami communicantes.

Components of the plexus are designated according to their location as roots, trunks, divisions and cords. Roots derive from the spinal nerves and are located in the posterior triangle of the neck. The trunks are named according to their relative position as the superior; middle and inferior. These trunks split into anterior and posterior divisions. The recombination of divisions forms cords which surround the axillary artery and are named according to their position.

The roots of the plexus, after leaving the intervertebral foramina, travel laterally atop the transverse processes of the cervical vertebrae. They emerge between the anterior and middle scalene muscles between which they descend toward the first rib and converge to form trunks of the plexus. The upper trunk is formed by the combination of nerve roots of C_5 and C_6. The middle trunk is the continuation of C_7 nerve root. The lower trunk is formed by C_8 and T_1 nerve roots. Behind the clavicle, each trunk divides into anterior and posterior divisions

(in relationship to the axillary artery). In the axila, recombination of divisions forms cords which surround the axillary artery and are named also according to their position. The lateral cord is formed by the upper two anterior divisions. The medial cord is formed by the lowest anterior division. The posterior cord is formed by the lowest anterior division (Collins 1976).

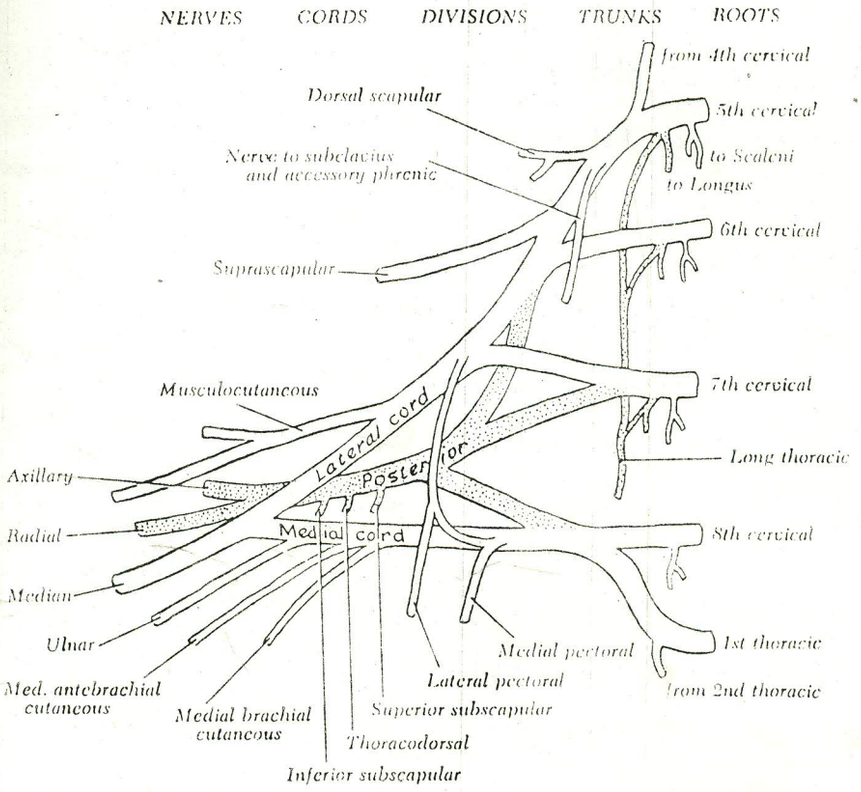

Fig. 1: Plan of the Brachial plexus (Collins 1976, pp 955)

1 - 4 METHODS FOR BRACHIAL PLEXUS BLOCK

1-4-1 SUPRACLAVICULAR BRACHIAL PLEXUS BLOCK (KULENKAMPFF TECHNIQUE)

This is the classic approach first described by Kulenkampff in 1911, which attempts to block the trunks of the brachial plexus as they cross the first rib in the posterior triangle of the neck (Moore 1965).

Applied Anatomy:

The first rib passes beneath the clavicle at about the union of its middle and inner thirds. At this point, the subclavian artery, which also emerges from between the anterior and medial scalene muscles, lies immediately anterior to the trunks of the plexus in the angle formed by the first rib and the clavicle. The dome of the pleura lies in the concavity of the first rib such that when a needle is passed so as to pass lateral to the rib or to hit the lateral border of the rib, there will be no chances of entering the pleura. Thus the first rib serves as a guide and also as a protective "backstop" in supraclavicular approaches to the brachial plexus (Collins 1976).

The Kulenkampff technique as applied today is that which has been modified by Macintosh and Mushin in 1944. This technique involves starting the injections into the lower trunk close to the Subclavian artery and working laterally. The description of the technique is given below.

Patient Positioning:

The patient is settled in the supine position with the head on a shallow pillow, the head is then rotated towards the contralateral side (side not affected) and the pillow pushed under the shoulder. The shoulder and arm of the affected side are depressed (This is conveniently done by requesting the patient to reach, with the tips of his fingers down the lateral aspect of the leg on the side of the injection).

Landmarks and Needle Insertion:

1. An intradermal wheal using a 23-gauge 5cm needle is raised 1 - 2cm above the mid-clavicular point. The landmarks of the mid-clavicular point can be sought for by any of the following criteria:-
   i) A point midway between the sternoclavicular and the acromioclavicular joints.
   ii) A point on the clavicle crossed by a line produced downwards from the external jugular vein, made prominent by blowing out cheeks or performing the valsalva manouvre.
   iii) A point just lateral to the pulsating subclavian artery which is often palpable.
   iv) A point lateral to the outer border of the scalenus anterior, which may be palpable under the lateral border of the sternomastoid muscle.
2. Then the subcalvian artery is palpated and compressed inward and downward by the index finger.
3. Finally the 23-Gauge 5cm needle is inserted downwards, inwards and backwards so that it is pointing to the spine of the second to fourth theracic vertebra (Atkinson et al 1977). It is then advanced gently and gradually toward the first rib. If the patient coughs, the needle is removed, since the cough is a sign that the pleura may have been stimulated or penetrated. If paraesthesias are felt before reaching the first rib, the needle is steadied and all the local anaesthetic sol tion is injected here, after a negative aspiration test.. If paraesthesias are not elicited after a few

needle insertions, the upper surface of the first rib is contacted. The rib is met with at a depth of from 3 to 5cm, depending on the adiposity of the subject and the absence of paraesthesia or contact with the rib at these depths denotes not only the plexus but also the rib has been missed (Bonica 1953). Once the first rib is contacted, the needle is then "walked" along the rib in anter-oposterior directions until paraesthesias are obtained. When they are elicited, the drug is injected all at one point. Thirty to forty millilitres of solution are used. If paraesthesias are not elicited an alternative method is to insert the needle just lateral to the subclavian artery as described above until it hits the first rib. After a negative aspiration test 10ml of solution are injected between the first rib and the skin. The needle is reintroduced on to the first rib, 1cm laterally to the first position, and 10ml similarly injected. Third and fourth injections are made each 1cm lateral to the last, and at each point 10ml are deposited (Atkinson et al 1977). This manouvre ensures that a bar of anaesthetic solution is deposited over an area between the first rib and the skin wide enough to ensure that it includes the brachial plexus. However injection of the anaesthetic solution without obtaining paraesthesias increases the probability of failure of block (Moore 1965).

Extent of Analgesia:

Anaesthesia develops rapidly if paraesthesias are obtained. One should allow 5 - 15 minutes interval for analgesia to be established. The following signs predict the rapid onset

of analgesia:-

Paraesthesias - These occur in the form of shooting or burning pains. Macintosh and Mushin thought that the elicitation of paraesthesia was not an essential part of the technique (Macintosh and Mushin 1954). Other authors independently think that positive evidence of correct placement of the needle tip should be searched for by elicitation of paraesthesias prior to injection. A paraesthesia is the reassuring forerunner of a successful block (Moore 1965, de Jong 1961). The presence of a sensation of warmth - in the arm of the side injected. This sensation is felt by the patient and the limb feels warm on touch.

"Pins and needles" sensation - There is a feeling of a "pins and needles" sensation in the injected limb.

Horners Syndrome - The presence of a Horners Syndrome indicates a successful block, although its absence does not mean the reverse.

Loss of Motor power - The loss of motor power follows analgesia. However loss of motor power depends on the concentration of the anaesthetic solution and for this reason with a low concentration of solution you may achieve analgesia without loss of motor power. Since motor fibers are more resistant than sensory fibers to local anaesthetics it follows that loss of motor power is a sure sign of loss of sensation (Macintosh and Mushin 1954).

Once the analgesia is achieved, operations on the lowerarm, hand, fingers and the upper outer arm below the insertion of the deltoid may be performed. Dislocated shoulders may

be reduced. Skin analgesia exists over the upper outer arm, the forearm and the hand.

The nerves that are part of the brachial plexus and are blocked by this technique include the axillary nerve (C_5C_6), the medial antebrachial cutaneous nerve (C_8,T_1), the musculocutaneous nerve ($C_5C_6C_7$),the radial nerve ($C_5C_6C_7C_8T_1$), the Ulnar nerve (C_8T_1) and the median nerve ($C_5C_6C_7C_8T_1$)..

The intercostobrachial nerve (T_2) innervates the medial and inner surfaces of the arm and is not part of the brachial plexus. When a pneumatic tourniquet is used, the intercostobrachial (T_2) and the medial brachial cutaneous (T_1,T_2) nerves should be anaesthetized. For prevention of tourniquet pain, anaesthesia is carried out by half ring subcutaneous infiltration with 10ml of local anaesthetic solution in the axilla. Also for procedures involving the inner upper arm or elbow as for prevention of tourniquet pain, an additional intradermal and subcutaneous local infiltration should be done in the axilla in a half ring form in order to block the intercostobrachial nerve (T_2) and the medial brachial cutaneous nerve (Moore 1965).

Operations on the shoulder also necessitate an additional intradermal and subcutaneous infiltrations in order to block the superficial cervical plexus, intercostobrachial nerve and the medial brachial cutaneous nerve. This is achieved by an intradermal and subcutaneuous local infiltration along the clavicle and border of the trapezius combined with the

half ring in the axilla. This blockade can also be achieved by a ring of local infiltration around the arm starting at the Coracoacromial junction (Moore 1965).

Complications of the Supraclavicular Block

With proper and careful technique the chances of getting complications are reduced to a minimum, however any of the following may occur:-

1. Pneumothorax -

   This is often secondary to the laceration of visceral pleura by the misplaced injection needle. The pneumothorax is not due to entry of air into the pleural space through the needle, but rather it leaks out of the lung through the pleural rent. The pneumothorax develops slowly after a supraclavicular block unless intermittent positive pressure ventilation is used. The incidence varies between; 0.5 percent and 4 percent. The incidence of this complication decreases as the performer becomes more experienced (Moore 1965).

2. Haemorrhage

   Bleeding results from the puncture of either the subclavian artery or the jugular vein. Haematomata may form and on rare occasions they have been found to cause permanent nerve damage (Wooley and Vandam 1959). However often times haematomas cause no serious consequences (Moore 1965).

3. Phrenic nerve paralysis

Higher up in the neck, the phrenic nerve is included within the fascial compartment as the brachial plexus components. Anaesthetic solution injection into the tissue surrounding the plexus can thus ascend and block the phrenic nerve. Such a block is usually harmless and causes no symptoms but may bring serious respiratory complications if there are pre-existing difficulties such as emphysema or kyphosis or when a general anaesthetic is to be administered (Moore 1965).

4. Horners Syndrome

This is due to stellate ganglian block. The injected local anaesthetic solution spreads upwards so that it involves the stellate ganglion. The signs of the syndrome clear as the block dissipates. It does not need any particular medical management. It occurs in approximately 70 - 90% of brachial plexus blocks when 50ml or more of local anaesthetic solution are injected (Moore 1965).

5. Drug Toxicity

Local anaesthetic drug toxicity is due to an inadvertent intravascular injection or when the maximum safe dose of the drug has been exceeded. Adherence to normal safe dosage and a slow injection with a prior negative aspiration test will reduce the chances of drug toxicity.

6. Neurological Complications

Nerve damage due to the injection needle is a rare complication. The needles used are of small gauge

and have a relatively blunt point rather than a sharp taper. The blunt needles will tend to push the nerve ahead of them and thus reduce the risk of neural damage. The small diameter of the needles makes damage to the nerves unlikely (Selander et al 1977).

7. Infection

Infection is a rare complication if the conventional techniques of sterilization of equipment and the aseptic technique are closely adhered during the blockade procedure. Local anaesthetics appear to have antimicrobial activity, being bacteriostatic and possibly bactericidal (Schmidt and Rosen Kranz 1970). This could contribute to the rare occurence of infection post block.

8. Other possible complications include subarachnoid injection and recurrent laryngeal nerve paralysis. These are however, rare complications (Snow 1977).

Contraindications to Supraclavicular Block

1. Infection on the injection site on the supraclavicular area.
2. Tumours on the supraclavicular area that might make anatomical identification of landmarks difficult and make needle insertion difficult.
3. Patient on anticoagulant drug therapy or one with a bleeding diathesis.
4. A pulmonary disease condition such as emphysema or Pneumonia on the side which the block is to be performed. This includes all chest conditions where lung function is compromised.
5. Active or recent neurological disease.

1-4-2 AXILLARY BRACHIAL PLEXUS BLOCK

The Axillary brachial plexus block was first described by Hirschel in 1911, when he attempted to reach the level of the first rib via the axilla using a 2½ inch needle. This method was unsuccessful. Pitkin 1920, modified Hirschel's technique by following the plexus through the apex of the axilla over the first rib to the transverse processes of C_6 and C_7. This approach requiring two insertions with 8 inch needles became unpopular and was abandoned. Later in 1949, Accardo and Adriani modified further on the Hirschel's technique, by confining the injections to the terminal nerves in the axilla and their method required four injections. More recently single injection techniques into the neurovascular sheath have evolved. Burnham in 1958 described the axillary perivascular technique of brachial plexus block. This was based on an earlier concept by Redding in 1921 that nerves in the axilla are enclosed in a sheath which favours diffusion of an anaesthetic solution such that the median, radial and ulnar nerves are all anaesthetized by single injection (Burnham 1958). The axillary perivascular brachial plexus block has been modified by several workers including de Jong 1961, and Erikson 1965. Eriksson's method involved the use of a venous tourniquet to prevent distal spread of the analgesic solution. Only one needle puncture is required.

Applied Anatomy:

The axillary artery is identified at the point of insertion into the humerus of the pectoralis major muscle anteriorly and the teres major - Latissimus dorsi group posteriorly. It lies on the medial aspect of the humerus and can be pressed against this bone. At this point the nerves supplying the hand, the forearm and most of the arm are arranged about the artery. The radial nerve lies behind the axillary artery; The median nerve lies infront and slightly above it; and the ulnar nerve lies infront and slightly below it. The musculocutaneous nerve arises from the lateral cord of the brachial plexus at the lower border of the pectoralis minor muscle. It pierces the coracobrachialis muscle and passes obliquely to the lateral side of the forearm as the lateral antibrachial cutaneous nerve.

The intercostobrachial nerve arises from T_2 and innervates the skin of the upper half of the medial and posterior part of the arm. The musculocutaneous and the intercostobrachial nerves are not within the neurovascular sheath around the axillary artery and are thus not easily anaesthetized by this technique (Moore 1965).

Landmarks:

i) The axillary artery - this forms the major landmark for axillary brachial plexus block. Its terminal portion is easily identified by pulsations in the apex of the axilla. At this point the axillary artery runs parallel to the axis of the humerus.

ii) Insertions of the tendons of pectoralis major and the latissimus dorsi - are another important landmark. A line connecting these two points lies just below the point where the cords of the brachial plexus give origin to the great nerves of the arm.

(iii) The Humerus bone - forms the third landmark and is the ""backstop" against which other soft tissue structures can be moved and steadied.

Techniques for Axillary Blocks

There are basically three types of procedures which may be applied to attain an axillary block of the brachial plexus. The classic technique, rarely used today is that described by Hirschel in which the needle is directed into the axilla parallel to the axillary artery in an attempt to place the anaesthetic solution as close to the level of the first rib as possible. Then there is the modified technique of Accardo and Adriani in which the needle is directed at right angles to the skin and the anaesthetic solution is injected around the four major terminal nerves of the plexus where they lie around the artery in the axilla. More recently, the axillary perivascular techniques have been introduced as a further modification over the technique of Accardo and Adriani. These new techniques are based on the identification of the axillary neurovascular sheath and then introduction of local anaesthetic solution into it by a single injection (Collins V J 1976).

(i) The Classic Approach (Hirschel)

The axillary artery is located by palpation and is then retracted inferiorly by the index finger. A subcutaneous wheal is made under the lower border of the pectoralis major muscle near its attachment to the humerus. A 10cm needle is then advanced parallel with the axis of the humerus along the outer wall of the axilla, deeply beneath the muscle. After a negative aspiration test, 10 to 15ml of the anaesthetic solution is injected. Then the axillary artery is pushed upward (toward the pectoralis major) by the index finger, and the needle inserted through another wheal raised a little below the first site of puncture. The needle is advanced deeply behind the artery in a direction parallel to the axis of the humerus, along the outer wall of the axilla, thus aiming at its apex so as to reach the radial nerve in front of the head of the latissimus dorsi muscle. If no paraesthesias are obtained, part of the solution is injected in the depth, and the rest while the needle is withdrawn, using 10 to 15ml of anaesthetic solution. If the needle impinges on one of the main nerves of the plexus during its advancement in the axillary space, it should be stopped and injection made without further movement. The axilla is massaged to hasten diffusion of the injected solution. If blood is aspirated, the needle is slightly withdrawn and redirected into another direction. Paraesthesias may be obtained duri ng the course of injection but they should not be sought for (Collins 1976).

ii) Modified Approach (Accardo and Adriani)

The axillary artery is palpated high in the axilla at the level of insertion into the humerus of the pectoralis major

and teres major muscles. It is retracted posteriorly with the thumb and index finger.

a) The median nerve is made easily palpable along the artery. A 2.5 - 5cm needle is inserted at right angles to the skin and humerus towards the median nerve. An attempt to elicit paraesthesias to the finger tips is made and an injection of 5ml of solution is made only after their elicitation.

b) The needle is withdrawn almost to the skin and then reintroduced at an angle of 45 degrees anterior to the direction of the first injection. The needle points to the insertion of the pectoralis major muscle. This manouvre is intended to inject the musculocutaneous nerve which at this point invariably is close to the artery. Paraesthesias should be elicited at the elbow joint. Five ml of anaesthetic solution are injected.

c) The needle is again withdrawn almost to the skin. The artery is now retracted anteriorly toward the upper surface of the arm. This exposes the ulnar nerve for palpation. It can thus be palpated on the under surface of the arm. The needle is then directed posteriorly (downward) at an angle of 45 degrees to the line of the original injection for the median nerve. Paraesthesias corresponding to ulnar distributions to fourth and fifth digits are elicited. Then five ml of anaesthetic solution are injected.

d) The radial nerve is the least accessible to infiltration because it is deepest and directly posterior to the axillary artery and thus not palpable. The needle is withdrawn almost to the skin while the artery is still

at an angle of almost 90 degrees to the direction of the first injection. Paraesthesias in the radial nerve distribution along the back of the hand should be elicited. Failure to elicit paraesthesias results in failure of blockade of the radial nerve. Five ml of anaesthetic solution is injected. Aspiration tests should precede each of the above injections and after completion of all the injections the site should be massaged gently for 5 minutes. To permit usage of a tourniquet, a subcutaneous ring of local anaesthesia, using 10ml of anaesthetic solution around the inner half of the arm is necessary to anaesthetize the medial brachial cutaneous nerve and the intercostabrachial nerve (Collins 1976).

(iii) The Axillary Perivascular Technique

This is yet a further improvement of the technique of Accardo and Adriani. With this method an axillary block follows if analgesic solution is injected periarterially into the fibrous neorovascular sheath.

Positioning of Patient - The patient lies supine with the arm abducted 90 degrees and externally rotated and with the elbow flexed. A tourniquet (Penrose drain) is applied tightly on the arm distal to the point of injection; this will prevent spread of the anaesthetic solution pheripherally. The tourniquet is removed 5 - 10 minutes following completion of block (Eriksson 1965). The skin in the axilla is shaved and cleaned.

Landmarks - The axillary artery is palpated as high as possible in the axilla, usually 2 - 4cm proximal to the

insertion of the pectoralis major and latissimus dorsi muscles. It is then fixed against the humerus by the anaesthesiologist's index finger.

Insertion of Needle - A skin wheal is raised and then a 23 - gauge 2.5cm needle is inserted until a distinct "click" is felt. This indicates the needle has penetrated the deep fascia forming the axillary sheath (neurovascular sheath) and its bevel is now within the neurovascular sheath. The needle is immobilized and the entire volume of anaesthetic is injected without an attempt to elicit paraesthesias (Burnham 1958). However newer modifications of the technique consider methods to ensure correct placement of the needle tip within the neurovascular sheath as necessary for a successful block (de Jong 1961, Eriksson 1965).

Correct placement of the needle within the neurovascular bundle is verified by:-

(a) Paraesthesias radiating down the arm to the fingers. In practice it is satisfactory to deposit anaesthesia solution when there are two paraesthesias on the median and ulnar side of the artery.

(b) Aspiration of blood into the syringe (de Jong 1961). If paraesthesias are obtained 30 - 40mls of 1% lidocaine with epinephrine 1:200,000 is administered following aspiration. If blood is aspirated, the needle is withdrawn gently until the aspiration of blood stops, and then the anaesthetic solution is administered. The small size of the needle decreases the possibility of haematoma formation.

Anaesthetic Solution - The adult requires 30 - 40ml of 1% Lidocaine with epinephrine 1:200,000 to ensure anaesthesia of the entire arm. In children 10 - 30 ml of 1% lidocaine with 1:200,000 epinephrine may be sufficient to produce analgesia. If smaller volumes must be utilized, the musculocutaneous nerve can be blocked separately; just above the elbow where the lateral antebrachial cutaneous nerve (terminal portion of the musculocutaneous nerve) emerges between the tendons of the biceps and brachioradialis muscles (de Jong 1965). When sufficient solution is injected (30 - 40mls) into the neurovascular compartment, it diffuses upwards to reach the lateral cord and thus include the musculocutaneous nerve (de Jong 1961).

The intercostobrachial nerve (T_2) is anaesthetized by subcutaneous injection of 3ml of anaesthetic solution over the axillary artery as you insert the needle to inject into the neurovascular sheath. If a tourniquet is applied or surgery on the arm at or above the elbow is to be carried out, a subcutaeneous ring of local anaesthesia, using 10ml around the inner half of the arm, is necessary to anaesthetize the medial brachial cutaneous nerve. This will also block the intercostobrachial nerve.

Extent of Analgesia

This approach does not give complete anaesthesia of the entire arm. There is complete analgesia below the elbow joint and there is good sympathetic block of the arm. Some branches of the brachial plexus are not accessible such as shoulder

branches which are not blocked (shoulder joint supplied by the suprascapular nerve C_5C_6). Thus reductions of dislocation of the shoulder joint cannot be performed under an axillary block. The intercostobrachial nerve should be blocked by an encircling Cuff of subcutaneous anaesthesia infiltrations.

Complications of An Axillary Block

The axillary brachial plexus block may be complicated by any of the following:-

i) Intravascular injection of the local anaesthetic solution. This is avoided by careful injection and frequent negative aspiration test before solution is injected.

ii) Injury to the nerves - This may present as a hypesthesia or paraesthesia. However such a complication is rare considering the small needle diameter that is used (de Jong 1961).

Selander et al, 1979 have shown that elicitation of paraesthesias was associated with an increase in postblock nerve lesions in axillary blocks.

iii) Injury to blood vessels leading to postblock haematoma formation. The needle's small diameter makes perforation of the vein or artery inconsequential (de Jong 1961).

iv) Infection - becomes a remote possibility if the aseptic technique is closely adhered to during the block procedure (de Jong 1977).

Indications of Axillary Block

The technique becomes particularly indicated in some situations including:-

i) When a supraclavicular technique cannot be done due to disease on the injection area like infection, injury or tumours.

ii) In pulmonary disease when the danger of pneumothorax and/or phrenic nerve paralysis must be avoided.

iii) When bilateral brachial plexus block is desired.

iv) For children with fractures of the arm.

Contraindications of Axillary Block

i) Local infection in the axilla

ii) Inflammatory response of the axillary lymphnodes to infection in the arm (lymphadenopathy).

iii) Patient on anticoagulant drug therapy or one with a bleeding disorder such as haemophilia.

1-4-3 THE SUBCLAVIAN PERIVASCULAR TECHNIQUE OF BRACHIAL PLEXUS BLOCKADE

This technique is based on the conception that the brachial plexus is included in a perivascular compartment together with the subclavian artery, enclosed by firm sheath continuous with the prevertebral sheath which surrounds the interscalene space. Unlike the multiple injections involved in the classic supraclavicular technique, this method involves deposition of anaesthetic into this potential space by a single injection (Winnie and Collins 1964).

All the techniques used in the supraclavicular approach to brachial plexus blockade the following features are part of the procedure (Winnie and Collins 1964).

i) The needles injected at a point lcm above the midpoint of the clavicle immediately lateral to the pulsations of the subclavian artery.

ii) The direction of injection is mesiad, caudad and dorsad.

iii) The first rib is used as a "backstop" and the needle is walked along the rib to obtain paraesthesias.

iv) The injections are multiple.

The anatomy of the brachial plexus sheath at this site, makes these features unnecessary. The subclavian perivascular space has a narrow anteroposterior dimension when viewed laterally and is triangular in shape when viewed from the front. Thus the supraclavicular techniques with their mesiad, caudad and dorsad direction enter the space at the lateral angle of the triangle where the width and depth is least. Injection at this site, may cause the needle to move out of the space even with slightest movement. With the multiple injections done in supraclavicular techniques the chances of the needle moving out of the space are increased. Introducing the needle at a higher level gives room for greater movement of the needle without leaving the space because the depth of the compartment is greater at this level. Applying a Caudal direction while introducing the needle improves the rate of success and reduces the possibility of pneumothorax. The direction of the needle insertion is parallel to the planes of the scalene muscles and because these muscles insert on the first rib, the position

of the rib and vessels are more precisely located than by any other method. The technique of walking the needle in an anteroposterior direction on the first rib in order to attain paraesthesias lacks a sound anatomical explanation, since the trunks lie one atop another and are not spread out horizontally over the rib. With the subclavian perivascular approach paraesthesias are usually obtained before the first rib has even been contacted (Winnie and Collins 1964).

Technique:

1. Position - The patient lies supine with the head turned to the side opposite that being anaesthetized and arms at the sides. The patient is requested to reach for his knee inorder to depress the shoulder and clavicle.

2. Anatomical Landmarks - Beginning at the lateral margin of the clavicular head of the stemocleidomastoid muscle, the index finger is rolled laterally across the belly of the anterior scalene muscle until the interscalene groove is palpated. The finger is then moved inferiorly along this groove until the pulsation of the subclavian artery is felt as it emerges from between the scalene muscles.

3. Needle insertion - While keeping the finger on the artery, a 1½ inch, 22-gauge needle is inserted superior to this point and is advanced in a direction that is directly caudad but neither mesiad nor dorsal.

This is in a direction that is dorsally tangential to the subclavian artery, while the level of insertion is high in the triangular interscalene space. The click may be felt as the sheath is penetrated by the needle if it is advanced slowly. When the needle is advanced further a paraesthesia will be obtained which confirms the presence of the needle in the perivascular space.

4. Anaesthetic solution Dose - Confirming the presence of the needle in the perivascular space, 40ml of solution are injected all at one site. While this technique results in more successful blocks than the classic supraclavicular method, it remained essentially the same as the former route since it carries the same risk of subclavian artery puncture and pneumothorax (Ward, 1974).

1-4-4: THE INTERSCALENE TECHNIQUE OF BRACHIAL PLEXUS BLOCKADE (WINNIE BLOCK)

Winnie 1970, introduced the third "perivascular" approach to the brachial plexus in addition to the axillary and subclavian perivascular techniques. The interscalene approach aims at depositing the local anaesthetic at the roots of the brachial plexus as they lie between the anterior and middle scalene muscles (Winnie 1970).

Applied Anatomy:

The nerves of the brachial plexus emerge from their grooved transverse processes and enter the interscalene space formed by the fascia covering the anterior and

middle scalene muscles. The greater part of this space is above the subclavian artery and the cupula of the lung. The injection enters the space at the level of C_6 vertebra. Injection at this high level in the neck offers even greater safety than injection by either the axillary or subclavian perivascular techniques. It carries the advantage that the anaesthetic solution is administered close to the origin of the nerves of the brachial plexus. In addition the musculocutaneous and axillary nerves, which come off high in the axilla, are anaesthetized (Winnie 1970, Ward 1974).

Technique:

1. Position - The patient lies supine with the face turned to the side opposite that being anaesthetized and arms at the sides.
2. Landmarks - To identify the clavicular head of the sternocleidomastoid muscle, the patient raises the head. The anaesthesiologist places his palpating fingers behind the tense prominent sternocleidomastoid muscle and the patient is asked to relax. The anaesthesiologist's fingers now lie on the belly of the anterior scalene muscle; when the fingers are moved laterally on this muscle, they fall into the interscalene groove, between the anterior and middle scalene muscles. The palpating fingers are now moved down the interscalene groove to the level of C_6, which is determined by extending a line directly laterally from the level of the lower

border of the cricoid cartilage. Another useful landmark is the external jugular vein which crosses the groove at this point.

3. Needle Insertion - At the identified point, a 23-gauge 3.8cm needle is inserted into the inter-scalene groove in a direction that is perpendicular to the skin of the neck in all planes, that is in a direction that is mostly mesiad but slightly caudad and dorsad. The needle is advanced until a paraesthesia is elicited or a transverse process of C_6 is encountered. Once a paraesthesias is elicited, the desired volume of anaesthetic is injected after a negative aspiration test has been confirmed. If the needle makes contact with the C_6 transverse process without producing paraesthesias, it is moved laterally until paraesthesias are obtained (Winnie 1970, Ward 1974).

4. Anaesthetic Solution and Dose - An injection of 30 - 40ml of the local anaesthetic solution is administered. The volume of injected anaesthetic solution is important since with large volumes, both cervical and brachial plexuses are anaesthetized.

5. Accessory block - As with all other perivascular techniques, the intercostobrachial (T_2) nerve should be anaesthetized in the axilla if a pneumatic tourniquet is to be used. This is accomplished by a half ring subcutaneous infiltration with 10ml of anaesthetic immediately superficial to the axillary artery pulse.

Advantages

The interscalene block of the brachial plexus has obvious advantages over more peripheral techniques for operations around the shoulder joint. It is suitable for surgical procedures on the acromioclavicular joint, the clavicle and for reducing dislocated shoulders. With a cranial spread of the anaesthetic solution to involve the cervical plexus and adequate caudad spread to anaesthetize all the brachial plexus, it can be used for operations on the shoulder joint itself.

The success rate of this technique is relatively high. Winnie 1970, found a 94% success rate after performing the technique in 200 patients. In his study of 34 interscalene block cases, ward 1974, demonstrated a 91% success rate.

With the interscalene technique the chances of puncturing the subclavian artery or the Cupola of the lung are minimized since the interscalene space into which the injection is made is high up in the neck above the subclavian artery (Winnie 1970).

Complications of the Interscalene Block

1. Injection into the vertebral artery: Every injection should necessarily be preceded by a negative aspiration test; since even small quantities of local anaesthetic injected into the vertebral artery produce large concentration in the cerebral circulation with convulsions (Korevaar et al 1979).

2. Epidural Blockade:

If the needle is directed horizontally or Cephalad there is a high risk of passing it between the vertebrae or through a paravertebral foramen into the epidural space. Cervical and thoracic epidural spread of anaesthetic solution have been reported after an interscalene technique of brachial plexus blockade (Kumar et al 1971).

3. Sub-arachnoid injection:

This is also a potential danger if the needle is not directed caudad but horizontally or cephalad, such that it goes in between the vertebrae and penetrates the dura. A case of total spinal anaesthesia has been reported after this blockade technique (Ross and Scarborough 1973).

With the needle always directed caudad, the incidence of complications should be low. With deeper needling a pneumothorax is a potential risk, but it is a remote possibility with this technique unlike the conventional supraclavicular technique (Winnie 1970).

1-4-5: <u>THE INFRACLAVICULAR BRACHIAL PLEXUS BLOCK</u>

This technique unlike the axillary and the supraclavicular approaches, attempts to reach the plexus from a point below the clavicle. Many workers including Babitski in 1918, Bazy and Biondin in 1935 and Dogliotti in 1939 had tried this approach of brachial plexus blockade but it was not adopted for popular use due its unreliability

of results (Macintosh and Mushin 1954). Of recent Raj et al 1973, have described an improved inflaclavicular approach to the brachial plexus.

In the infraclavicular approach, the needle is inserted 2cm below the midpoint of the inferior border of the clavicle and the anaesthesiologist using a modified nerve stimulator locates the brachial plexus with a lateraly directed needle from this insertion point. Thirty-five ml of local anaesthetic solution are injected at this site and result in satisfactory analgesia (Raj et al 1973).

This technique has been modified by Sim, 1977, whereby the needle insertion is made at a more lateral point in the interval between the coracoid process of the scapula and the inferior border of the clavicle. In this modification like in the earlier one by Raj et al, a nerve stimulator is used to locate the brachial plexus. Contact with the plexus is reached at a distance 2 - 3cm from the skin wheal. Then thirty-five ml of local anaesthetic solution are injected all at one point.

Advantages:

1. It is used when the axillary approach or approaches to the plexus in the posterior triangle are contraindicated for various

reasons (e.g. Difficulties in patient positioning, fractures and infections).

2. Better than the axillary approach, since it deposits the anaesthetic solution more cephalad in the axillary sheath and thereby assures block of the musculocutaneoous nerve.

Disadvantage

Pneumothorax is a potential risk if the needle is directed medially in error.

1-4-6: THE "CORACOID APPROACH" FOR BRACHIAL PLEXUS BLOCKADE

Whiffler 1981, described yet another approach towards attaining brachial plexus blockade. His, is essentially a variation of an infraclavicular technique which attempts to block the plexus within the axillary sheath by approaching it through the anterior aspect of the axilla.

Applied anatomy - At the level of the coracoid process the three divisions of the brachial plexus form the lateral, posterior and medial cords. The cords of the plexus together with the axillary artery and axillary vein, are enclosed in the axillary sheath forming a neurovascular bundle. The inter-costo-brachial nerve runs in close proximity to the axillary sheath. This therefore could make an ideal site for brachial plexus blockade (Whiffler 1981).

The Coracoid block as described by Whiffler 1981, is presented below.

Patient Positioning:

The patient lies supine with head turned to the side opposite to that being anaesthetized. The shoulder on this side is depressed and arm abducted approximately 45° from the chest wall.

Landmark identification:

The midclavicular point is identified and the subclavian artery palpated. The artery is traced laterally until it dissapears behind the clavicle and this site is marked with a skin marker as X_1. The coracoid process is then identified and marked with a skin pen. The axillary artery is palpated with the index finger as high as possible in the axilla. The thumb is placed on the anterior surface of the chest wall over the site at which the index finger palpated the axillary artery. This point is marked with a skin pen as X_2. The depth at which the axillary sheath and contents lie can then be gauged by estimating the distance between the thumb and the index finger and this gives an indication of the depth to which the needle has to be inserted. Points X_1 and X_2 are then joined by a skin pen. This line passes immediately inferior and medial to the coracoid process.

Needle insertion:

The skin over the coracoid process is then washed by antiseptic solution. Using a 21-gauge 51-mm needle, the skin is punctured inferomedial to the coracoid process and the line joining X_1 and X_2 is transected. The needle is advanced to a depth which had previously been estimated by the distance between the thumb and index finger. The needle is kept at right angles to the skin. After a negative aspiration test, some 12ml of local anaesthetic solution is injected. The needle is withdrawn 1cm and the procedure of aspiration and injection repeated.

This procedure may be repeated twice in a muscular person (36 mls of solution) and once in a thin patient (24 mls of solution). This procedure distributes the local anaesthetic solution around the neurovascular bundle. If there is doubt on whether the needle has penetrated the axillary sheath, it is withdrawn up to the skin and then re-introduced in a slightly angled direction either inferiorly or superiorly to the first injection. Care is taken not to exceed the total calculated safe dose of the local anaesthetic drug. The onset of analgesia is slightly longer than in the standard supraclavicular technique, the average time being 10 - 20 min. Sensory block extends from C_5 - C_6 to T_2. The whole of the axilla is thus anaesthetized and it is not necessary to block the intercosto-brachial nerve (Whiffler 1981).

Advantages of the Coracoid block:

1. There is no phrenic nerve paralysis as in the supraclavicular technique and can thus be used in bilateral brachial plexus blocks.
2. There is no possibility of inducing a pneumothorax
3. The intercosto-brachial nerve is blocked, hence no need arises to do an accessory block for this nerve.
4. It is superior to the axillary approach, since its introduction of anaesthetic solution avoids the axilla, which is a potentially septic area (Whiffler 1981).

1 - 5: INDICATIONS:

Brachial plexus blockade anaesthesia is used in upper extremity surgery or manipulation particularly when the administration of a general anaesthetic drug is contraindicated for various reasons or when the patients cooperation is needed during the procedure.

It has also been of therapeutic use when severe pain of the upper extremity such as herpes zoster has been relieved by the block. It also confers good immediate postoperative analgesia without resort to narcotic analgesics with their attendant risks (Moore 1965).

PART 2

LITERATURE REVIEW ON LIDOCAINE

PART 2: LITERATURE REVIEW ON LIDOCAINE

2 - 1 INTRODUCTION:

Nerve conduction can be altered by different means such as mechanical trauma, low temperature, anoxia and a variety of other irritants such as alcohol and phenol. In clinical practice pharmacologic agents usually employed produce a transient and completely reversible state of anaesthesia in the area where loss of sensation is desired (Covino, 1972).

2 - 2 HISTORY OF LOCAL ANAESTHETICS

The present day local analgesia dates back about 100 years when Carl Koller introduced cocaine into medical practice in the year 1884 (Koller, 1941).

Cocaine is a product of the leaves of Erythroxylon coca, a tree that grows in the Andean foothills of Bolivia and Peru. Here the mountain dwellers have been chewing the leaves for centuries because of their euphoriant effects. In 1885, Gaedicke extracted the alkaloid erythroxylin from the Erythroxylon coca leaves. Finally in 1860, a chemist Albert Niemann isolated Cocaine from the erythroxylon extract (Koller 1941, McAuley 1966).

The anaesthetic potential of cocaine was demonstrated by Carl Koller, a Viannese ophthalmologist. In 1884 he applied cocaine on the conjuctiva of the human eye and produced local anaesthesia (Faulconer and Keys, 1965). This discovery prompted the use of cocaine in many other clinical disciplines like nerve

block, infiltration and even spinal anaesthesia. The fast adoption was encouraged by the almost simultaneous discovery of the hypodermic syringe by Von Neuner in 1827 (McAuley 1966). Nerve conduction blockade in man was first described by William Stewart Halstead just a year after Koller's discovery of local anaesthesia. His first case was a mandibular nerve blockade (Olch, 1975). In the same year (1885), Leonard Corning a New York neurologist while experimenting with cocaine on spinal nerves of dogs, by sheer luck entered the subarachnoid space. He repeated this intradural injection of cocaine and called it spinal anaesthesia and suggested its possible use in operative surgery. However it was 1898, when August Karl Gustav Bier did and reported true spinal anaesthesia (Scott and Thornburn, 1975).

Although, the local anaesthetic technique was gaining ground, the toxicity and addictive properties of the drug(cocaine) used, was a major deterrent. It is reported that Halstead himself became a cocaine addict as a result of experimenting with the drug on himself (McAuley 1966, Olch 1975). Folk in 1890, had reported 176 cases of acute intoxicatinn due to cocaine, of which 10 were fatal (Gray, and Geddes 1954). Cocaine's adverse effects prompted a continued chemical search for less toxic and non-addictive local anaesthetics. In 1895, Willstatter et al, elucidated the chemical stnucture of cocaine as being a benzoic acid ester of the alkaloid ecgonine. This limited the search to

benzoic acid esters. An infinite number of synthetic substitutes was produced but most of them were toxic and irritating, until 1904 when Alfred Einhorn synthesized procaine. Procaine was less toxic than cocaine and lacks its addictive properties (de Jong 1977).

In 1943, some fifty years later, Lofgren, a Swedish chemist synthesized Lidocaine (Lignocaine, Xylocaine). This new drug, unlike procaine was an amide compound (Lofgren 1948). Lidocaine, had advantages over both cocaine and procaine. Unlike cocaine it is not addictive and has only one fifth the toxicity of cocaine. Lidocaine, unlike procaine does not show hypersensitivity reactions and is three times more potent than procaine. It is however, 1.5 times as toxic as procaine (Collins, 1976). In clinical use today are many synthetic amide linked local anaesthetic drugs which do not possess cocaine's potential for habituation. Lidocaine ever since its discovery has been widely used both in surgery and medicine.

2 - 3: ANATOMY AND PHYSIOLOGY OF IMPULSE TRANSMISSION

2-3-1: THE NERVE AND AXON MEMBRANE:

A peripheral nerve is made up of several axonal groups or fascicles. Each axon has a connective tissue covering called the endoneurium. Each group of axons (fascicle) is further covered by another connective tissue layer, the perineurium. The entire nerve is covered by a sheath, the epineurium (Ganong 1979).

Non myelinated axons are encircled by the schwann-cell sheath, while the myelinated ones have a core of myelin

layer in between the axolemma and the schwann-cell sheath. Thus for a local anaesthetic drug to reach the axonal membrane site, it has to pass through four connective tissue barriers in cases of non-myelinated nerves and five barriers in case of myelinated nerves (Miller 1981).

The axon membrane forms a 75-Angstroms thick boundary between the axoplasm interior aspect and the extracellular fluid space on the exterior. The earliest detailed structure of the axonal membrane (plasma membrane) was suggested by Danielli and Davson 1936 and by Robertsnn in 1959. These, introduced the idea of biological membranes consisting of a bimolecular lipid layer, sandwiched between protein monolayers. At present the widely accepted model is the "Fluid mosaic Model" as suggested by singer and Nicholson 1972. This model potrays the image of a membrane as being a bimolecular lipid matrix made of long chain fatty acids with polar heads (phosphatidyl choline and phosphatidyl inositol). The long chains are oriented towards the interior of the bilipid layer. The polar heads are exposed to two aqueous phases one on the extracellular space and the other towards the cytoplasm on the interior aspect. Within the bilipid matrix are embedded globular proteins. Some of these proteins are located on the interior aspect and some on the exterior aspect jutting out over the polar heads. Other protein structures extend the whole thickness of the bilipid matrix from the external surface to the cytoplasmic side (i.e. through and through proteins). The hydrophillic, charge bearing

portions of proteins are oriented to the aqueous environment that bathes the exterior of the cell and the aqueous cytoplasm. The hydrophobic protions meet and interact with the lipids of the membrane in the bilipid layer (Singer and Nicholson 1972).

The embedded membrane proteins sub serve several functions. Some proteins function as passive channels for ions that can be opened or closed by changes in the conformation of the protein. There are proteins that function as pumps - actively transporting ions across the membranes. Other proteins function as receptors that bind neurotransmitters and hormones initiating physiologic changes inside the cell. Some proteins function as enzymes catalyzing reactions at the membrane surfaces. The remainder are structural proteins of the membrane (Ganong 1979).

Some membrane proteins therefore represent "ionic-channels" responsible for transmembrane conductance of potassium and sodium which are essential to produce changes in the resting membrane potential that induces propagation of the nervous impulse. Local anaesthetic receptors are thought to be located on these ionic channels (Miller 1981).

The Axonal membrane is a dynamic structure and its constituents are being constantly renewed at different rates. For example glycoproteins are known to move laterally in the membrane (Ganong 1979).

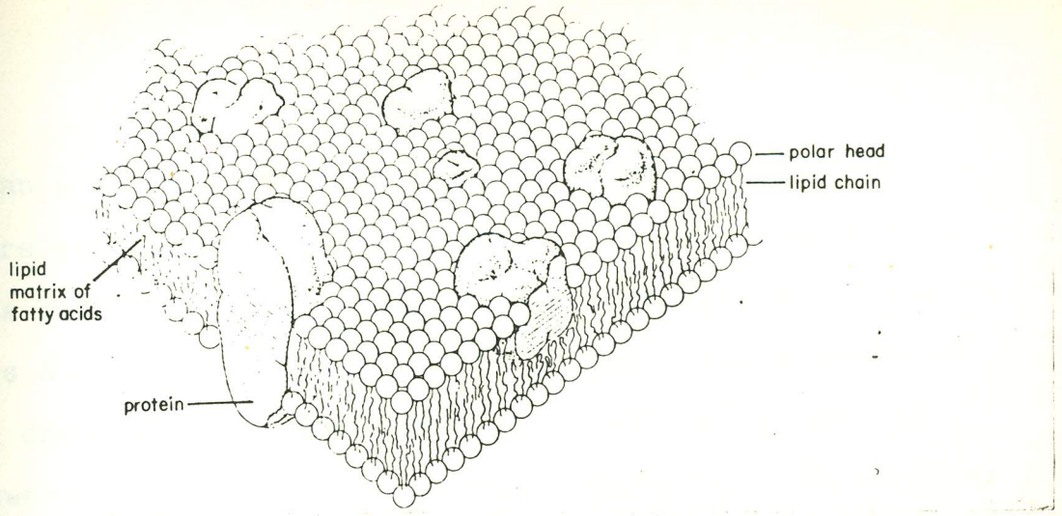

Fig. 4: The Singer-Nicholson Model - depicting a relatively fluid lipid bilayer in which proteinacious structures are embedded. Some of the proteins which project all the way through the membrane may constitute the essential portions of ionic channels responsible for transmembrane sodium and potassium conductance. (Singer and Nicholson 1972).

2-3-2 THE RESTING MEMBRANE POTENTIAL (RMP)

When a microelectrode connected to a cathode Ray oscilloscope is inserted into a nerve fiber (giant squid axon), a potential difference can be recorded between it and a second electrode placed in the extracellular fluid. Such a potential, called the resting membrane potential lies within 60 to 85 millivolts, the interior being negative to the exterior (Ganong 1979).

The axonal membrane is a semipermeable membrane, such that it is permeable to K^+ and Cl^-, hardly permeable to Na^+ (50 - 100 times less permeable to Na^+ than to K^+) and virtually impermeable to the

organic anions. Because of this membrane behaviour, there is an asymmetrical distribution of the permeable ions between the two sides of the semipermeable membrane. This asymmetry in distribution of the ions, results in the creating of a difference in electrical potential between the two sides. In addition to this, there is an energy dependant mechanism (The sodium - Potassium pump) which extrudes Na^+ ions against a concentration gradient while pushing K^+ towards the cell interior. More Na^+ ions are extruded than K^+ are pushed in by the pump. The sodium pump therefore, restores and maintains the resting unequal distribution of ions across the membrane (Ganong 1979). The high intracellular concentration of potassium is maintained by the attractive forces of the negative charges, mainly on proteins within the cell which counterbalances the tendency of potassium inns to diffuse out of the cell by passive movement along a concentration gradient and across a freely permeable membrane (Covino and Vassalo 1976). It has been shown that the resting membrane potential arises largely from the potassium ion concentration gradient. When the axoplasm is squeezed out and replaced by a solution of potassium salt, the axon still maintains a resting potential close to normal and continues to conduct nerve impulses. Hence a nerve at rest behaves as a "potassium electrode (Ganong 1979, Covino and Vassalo 1976).

2-3-3 Action Potential

An impulse or excitation causes depolarization of the membrane. When the membrane becomes depolarized some

initial 15mV, the rate of depolarization increases. This point is the firing or threshold potential level. Thereafter the oscilloscope tracing rapidly reaches and overshoots the zero-potential line to about +35mv. It then reverses and falls rapidly to the resting level when repolarization is about 70% completed the rate of repolarization decreases and the tracing approaches the resting level more slowly. The sharp rise and rapid fall are the "spike potential" of the axon, and the slower fall at the end of the process is the "after-depolarization". After reaching the previous resting level, the tracing overshoots slightly in the hyperpolarizing direction to form the small but prolonged after-hyperpolarization. The whole sequence of potential changes is called the "Action Potential". The action potential duration is about 1 millisecond. Depolarization takes about 0.3 millisecond while the repolarization phase lasts for 0.7 millisecond (Ganong 1979).

Subthreshold stimuli do not produce an action potential but instead produce localized depolarized potential changes that rise sharply and decay exponentially with time. Hence these do not trigger an impulse transmission.

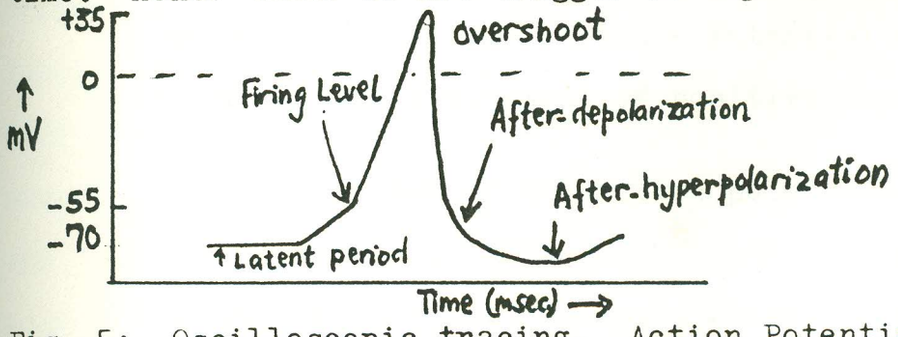

Fig. 5: Oscilloscopic tracing. Action Potential (spike potential recorded with one electrode inside cell (Ganong 1979, pp 33)

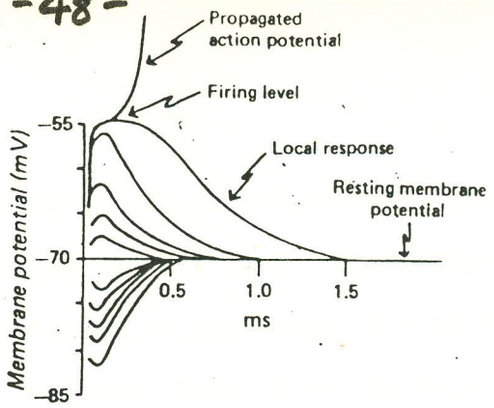

Fig. 6: Electrotonic Potentials and local response. The changes in the membrane potential of a neuron following application of stimuli of 0.2, 0.4, 0.6, 0.8 and 1.0 times threshold intensity are shown superimposed on the same time scale. The stimulus of threshold intensity was repeated twice. Once it caused a propagated action potential;(top line) once it did not (Ganong 1979 pp.35)

2-3-4 IMPULSE PROPAGATION

During the action potential; the polarized state of the nerve membrane is reversed. At the active site (impulse site) there is a reversal of the potential when the inside becomes positive and the outside negative. This causes positive charges from the resting site ahead of the action potential Iimpulse) to flow into the negative area represented by the action - Potential ("Current Sink"). This movement of positive charges from the area ahead of the action potential, depolarizes the membrane at this site. Such depolarization initiates a local response, which if it exceeds the threshold level, a propagated response occurs which in turn depolarizes the membrane in front of it.

This sequence of events (the impulse) moves along the nonmyelinated axon to its end. Once initiated, a moving impulse does not depolarize the area behind it to firing level because this area is refractory. Depolarization in myelinated axons jumps from one node of Ranvier to the next because myelin is an effective insulator and current flow through it is negligible. This jumping of depolarization from node to node is called saltatory conduction (Ganong 1979).

Ionic Basis of Impulse Propagation

On excitation a neuronal membrane changes its ionic conductance characteristics. Its Na^+, K^+ and Cl^- conductance increase and these ions passively traverse the membrane depending on their concentration gradients. When the membrane potential after excitation exceeds the firing threshold, there is a sudden great increase in Na^+ conductance into the cell so that the influx lowers the resting membrane potential. This further increases the Na^+ permeability. The resulting Na^+ influx causes the sudden depolarization producing the spike potential. Sodium permeability starts to return to the resting value during the rising phase of the spike potential and Na^+ conductance is decreased during repolarization. This occurs due to the reversed electrical gradient for sodium and the reversed membrane potential. Repolarization is also produced by the increase in K^+ permeability that follows the increase in Na^+ permeability. K^+ permeability starts gradually and attains a peak during the falling phase of the action potential. The outward movement of

K^+ causes a net transfer of positive charge out of the cell and thus completing repolarization. During the after-hyperpolarization phase, the sodium-potassium pump extrudes Na^+ ions and pumps in K^+ ions thus restoring the resting membrane potential and maintaining the normal unequal distribution of diffusible ions (Ganong 1979).

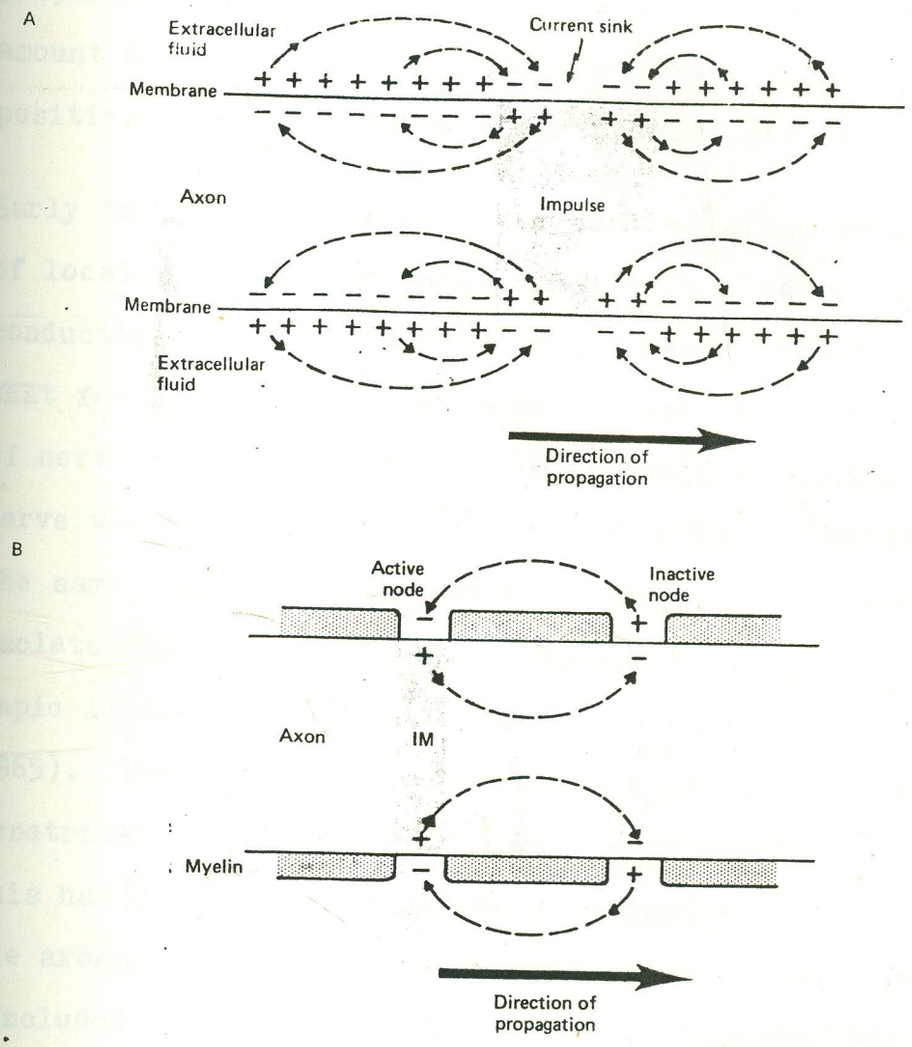

Fig. 7: Local Current flow around an impulse in an axon. The current flow is represented as movement of positive charges. A = situation in non myelinated nerves B = situation in Myelinated nerves (Saltatory conduction). IM = Impulse (Ganong 1979 pp 36).

2-4: MECHANISM OF ACTION OF LOCAL ANAESTHETICS:

2-4-1: THE ACTIVE FORM OF LOCAL ANAESTHETIC

For convenience, local anaesthetics are marketed as the hydrochloride salts which are soluble in water but insoluble in organic solvents. The pKa of the drug preparation and the tissue pH will determine the amount of drug that exists as free base or as the positively charged cation when injected into tissue.

Early in 1958, it was observed that alkaline solutions of local anaesthetics more effectively blocked nerve conduction (Shanes, 1958). It was demonstrated later that for a nerve with an intact sheath the rate of onset of nerve blockade increased as the medium bathing the nerve was made more alkaline (Ritchie et al 1965). The same people also demonstrated that for a desheathed isolated nerve, the onset of impulse blockade was more rapid if the bathing medium was acidic (Ritchie et al 1965). They thus concluded that the uncharged base penetrates the lipophilic nerve sheath easily and once this has occured the positively charged cation binds the axonal membrane to block conduction. They further concluded that for effective impulse blockade, both forms of local anaesthetics must be present (i.e. the uncharged base and the charged cation). It was further demonstrated that the quartenary derivatives of lidocaine (which bear a permanent positive charge) and their tertiary amine analogues are both effective in causing conduction blockade when applied on the interior aspect of the nerve membrane. This showed that the cation was the

effective form of the local anaesthetic (Narahashi et al 1969, Frazier et al 1970, Narahashi et al 1970). These observations by Ritchie et al 1965 and Narahashi et al 1969, 1970 did not explain the local anaesthetic action of neutral compounds like benzocaine, N-butanol or benzylalcohol.

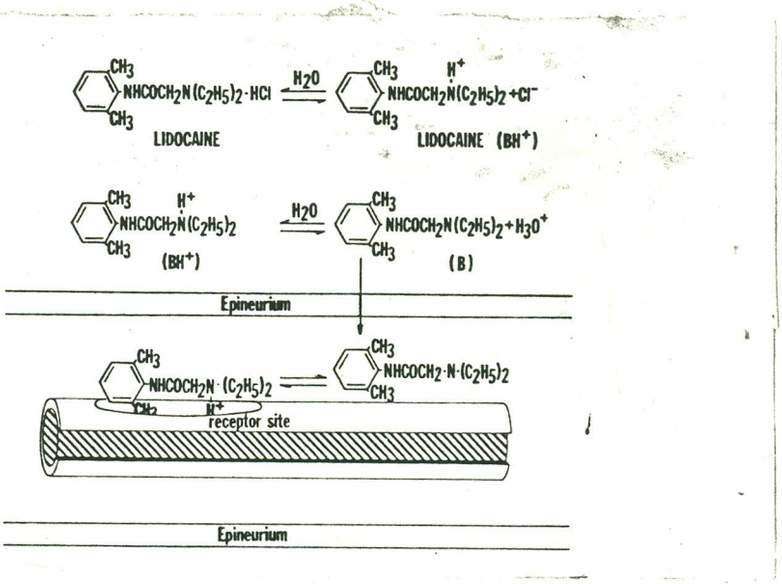

Fig. 8: Diffusion of the base form of local anaesthetic agent across epineurium and subsequent binding of cationic form with receptor site at nerve membrane.

2-4-2 THE BLOCKING PROCESS

Local anaesthetics mainly act by preventing the depolarization phase of the impulse conduction along the azonal membrane. They inactivate or severely impede the sodium ion flux into the cell, but have minimal effect upon the conductance of potassium. The influx of sodium ions is under the control of calcium ions. The increased sodium conductance results from the release of calcium bound to the nerve membrane. Local anaesthetics interfere with calcium release. The postulated sequence of events to explain the action of local anaesthetic drugs is as follows:- The local anaesthetic displaces calcium

displaces calcium ions from a specific receptor in the cell membrane and takes its place. This leads to a reduced permeability of the membrane for sodium, followed by a slower rate of depolarization of the nerve membrane, and a reduced amplitude of the depolarization potential. Threshold, or firing level is not reached, a propagated action potential does not occur, and impulse conduction is blocked (Covino and Vassallo 1976).

2-4-3 THE MEMBRANE SITE OF ACTION OF LOCAL ANAESTHETICS

There are several theories suggesting the site of action of the local anaesthetic drugs.

(i) The local anaesthetic Receptor Theory:

There is experimental evidence suggesting that local anaesthetics prevent sodium influx by their action on specific receptors that control gate mechanisms responsible for conductance changes in sodium channels. There are two receptor sites identified, located on the external and internal aspects of the sodium channel (Stritchartz 1976, Hille 1977).

The External receptor site has been shown to be blocked by two biotoxin substances, tetrodotoxin (TTX) and saxitoxin (SXT). These substances carry a permanent positive charge. The Internal receptor was shown to be one amenable to blockade by clinically useful local anaesthetics in their charged forms and also by their quartenary (charged) derivatives when the latter are applied on the

the membrane lipid as the uncharged base (Hille B 1977). Narahashi and Frazier 1971, in their study on active forms of local anaesthetics, showed that approximately 90% of the blocking action was caused by the base form.

The charged biotoxins, saxitoxin and tetrodotoxin must reach the internal receptor via the external opening of the sodium channel, since they do not cause blockade when applied on the internal aspect of the neuronal membrane (Hille 1977).

(ii) The Surface Charge Theory:

This hypothesis suggests that the lipophilic portion of the local anaesthetic molecule binds to non-specific ubiquitous sites within axonal membrane lipids, leaving the protonated positively charged amine portion of the molecule on the external surface of the membrane. The accumulation of positive charge will neutralize the relative electronegativity of the external membrane surface resulting in an increase in the transmembrane potential, leaving the intracellular resting potential unchanged. Sufficient increase in the transmembrane potential would inhibit the ability of an electrotonic current from an adjacent unanaesthetized portion of the nerve membrane to depolarize the treated area to its threshold for firing. Conduction blockade would then result. This theory does not explain the activity of neutral drugs such as benzocaine that do not exist in a charged form (Covino and Vassallo 1976).

(iii) The Membrane Expansion Theory:

This theory proposes that there is an interaction between the hydrophobic local anaesthetic molecule and the membrane lipids resulting in membrane expansion which causes a conformational change in the lipoprotein matrix of the membrane. The conformational change in the protein molecules that make up the sodium channels results in the reduction of the size of these channels, thereby preventing sodium conductance and inhibiting depolarization. This theory explains the local anaesthetic activity of compounds that remain uncharged at physiological pH - but does not explain the activity of charged anaesthetic molecules (Covino and Vassallo 1976).

2-5 CHEMISTRY OF LIDOCAINE

Lidocaine was first synthesized by Lofgren in the year 1943 and was introduced for clinical use by Gordh in 1948. It was an amide compound unlike its predecessors which were ester compounds.

2-5-1 Chemical Name and Structure

Lidocaine is 2-diethylaminoacet-2,6-xylidide. It is essentially an amide resulting from the reaction of an acid (diethylaminoacetic acid) and an ammonia-containing substance, xylene. Chemical structure:-

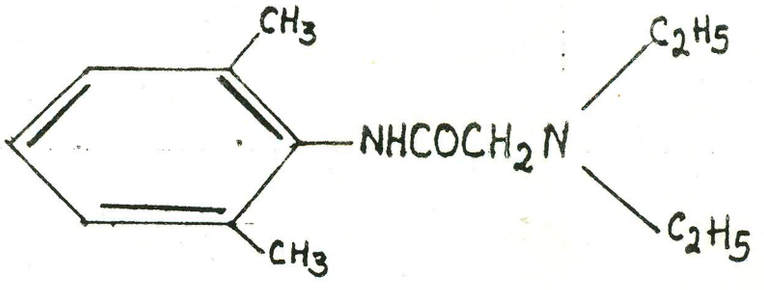

Fig. 9: Lidocaine (2-diethylaminoacet-2,6-Xylidide)

2-5-2 Structure Activity Relationships:

Lidocaine chemical structure like other local anaesthetics consists of three essential portions vital for its chemical and physical properties. There is the unsaturated (aromatic) ring head, the tertiary amine tail and an intermediate chain. The tertiary amine portion is separated from the aromatic ring by a distance of 6 - 9 angstroms by the intermediate chain (de Jong 1977). Lofgren 1948, suggested the general formula, "AROMATIC RESIDUE - INTERMEDIATE CHAIN - AMINO GROUP". The intermediate chain is an amide (-CNH-) linkage for the amide Compounds and an ester (-CO-) linkage for the ester compounds. It is essential for anaesthetic potency, since its removal results in loss or decreased activity. The flexibility of the intermediate link is essential for the drugs reaction to membrane receptors. It also predetermines the drugs course of biotransformation, since amides have a different biotransformation route from amino esters (de Jong 1977).

The Aromatic ring portion contributes the lipophilic character (lipoid solubility) necessary for local anaesthetic activity, while the tertiary amine tail is hydrophilic and provides the water solubility necessary for the local anaesthetic (Covino and Vassalo 1976, de Jong 1977). The local anaesthetic base (the tertiary amine) is not soluble in water. However, being a weak base it readily combines with acids to form water soluble salts. Lidocaine like other local

anaesthetics is dispensed for injection in the form of a salt (usually the hydrochloride) dissolved in sterile water or saline (Goodman and Gilman, 1975, de Jong 1977). In solution the salt ionizes to yield a quartenary amine cation plus an acid anion. The quarternary amine further dissociates into uncharged tertiary amine base and a hydrogen ion. Thus:

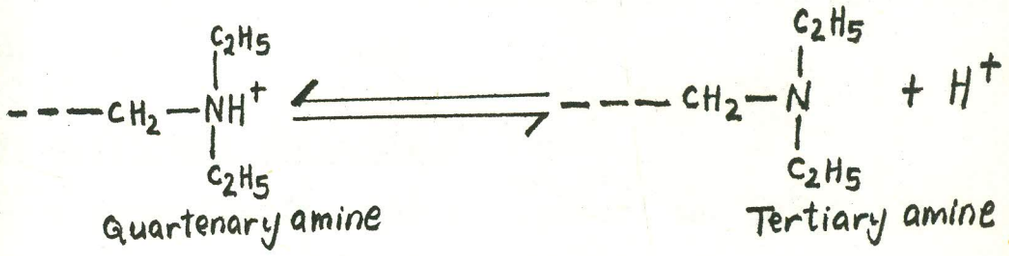

Fig. 3: Dissociation of a quartenary amine in an aqueous medium. The quartenary amine (cation) carries a positive charge, whereas the tertiary amine (anaesthetic base) is uncharged (de Jong 1977) Lidocaine therefore, exists in aqueous solution as a mixture of two forms, the uncharged base form (B) and the charged ionic or ;acid form (BH^+) according to the equilibrium:

$$BH^+ + H_2O \rightleftharpoons B + H_3O^+$$

The dissociation into cations depends on the pKa of the drug and the pH of the medium. The amounts of the two forms of lidocaine that coexist insolution is determined by the expression

$$pH = pKa - \text{Log} \frac{[BH^+]}{[B]}$$

The ratio between the two forms is defined by the value of pKa and pH of the solution. Therefore the pH

of the medium into which the local anaesthetic is deposited has an influence on drug activity by changing the proportions of basic or protonated forms of the drug. Lidocaine with a pKa of 7.85 is about 65% ionised at physiological pH. Both forms of the drug are essential to effect impulse blockade along neural membranes (Ritchie and Greengard 1961, Naharashi, Frazier and Yamada 1969).

2-5-3 Physicochemical Properties:

Lidocaine is freely soluble in water; the pH of a 1% solution in 0.9% saline is 6.5 - 7.0.

It has a pKa of 7.85

Lidocaine is sterilized by autoclaving or boiling; Crystals may be autoclaved for 6 hours or subjected to multiple autoclaving without loss of potency.

It is not irritating to tissues.

Systemic toxicity is one-fifth that of cocaine and 1.5 times that of procaine.

It is three times the potency of procaine.

2-6 PHARMACOKINETIC ASPECTS OF LIDOCAINE

2-6-1 ABSORPTION

Lidocaine is administered by injection into a depot site for attainment of regional anaesthesia. It is also given by intravenous route for intravenous regional anaesthesia, for control of ventricular arhythmias, as an anticonvulsant or as an adjunct to general anaesthesia. Absorption from a depot site is slow,

taking 15-30 minutes to attain peak blood levels, whereas by the intravenous route peak levels are attained immediately (Tucker and Mather 1979). Absorption from a depot site is determined by the following factors:-

Injection site:- The absorption of the drug will depend on the local perfusion of the site and the tissue binding characteristics of the drug. Peak blood levels attained vary directly with the local vascularity of the site. It has been found that the systemic absorption of local anaesthetic as reflected by maximum blood level of the drug, generally occurs in the following decreasing order according to the site of injection.
Intercostal > Caudal > Epidural > Brachial plexus > sciatic-femoral block. The lowest drug blood levels are attained after subcutaneous administration (Covino and Vassallo 1976).

Dosage:- The peak local anaesthetic blood levels are directly related to dosage, regardless of the injection site or the volume of solution employed. There is a linear relationship between the amount of drug administered and the resultant peak anaesthetic blood level (Covino and Vassallo 1976).

Addition of Vasoconstrictors:- Vasoconstrictor substances in optimal amounts are added to local anaesthetic solutions prior to administration. The reasons for addition of the vasoconstrictor are, first it decreases the rate of absorption from the various sites and in so doing reduces

the potential of systemic toxicity. The blood levels of the local anaesthetic are lowered by approximately 33 per cent when adrenaline is used. Secondly, the vasoconstrictor is used to prolong the duration of action of the local anaesthetic.

The combination of reduced systemic absorption and enhanced uptake by the nerve results in prolongation of the anaesthetic effect by roughly 50 percent (Covino and Vassallo). However the vasoconstrictors are less useful in prolonging the effects of the highly lipid soluble long acting drugs like bupivacaine and etidocaine because they are highly tissue bound and their potent vasodilating properties counteract the vasoconstricting effects of adrenaline (Covino and Vassallo 1976).

Pharmacological characteristics of the drug:-

The systemic absorption of Lidocaine and mepivacaine is greater than that of the more lipophillic agents, bupivacaine and etidocaine, probably because of the greater tissue binding of the latter drugs at the site of injection (Covino and Vassallo 1976, Tucker and Mather 1979). Further, the highly lipid soluble drugs (bupivacaine and etidocaine) have a more pronounced vasodilator tendency than lidocaine and mepivacaine.

2-6-2 DISTRIBUTION

The blood levels of lidocaine following absorption from the site of injection is a function of both the rate of distribution from the vascular compartment to tissue compartments and of elimination via metabolic and excretory pathways. Lidocaine is widely distributed throughout the body tissues

but the relative concentration in different tissues varies. An initial rapid distribution phase represents uptake into highly perfused organs (brain, liver, kidney, heart). The slower distribution phase corresponds to uptake by the intermediately perfused tissues (muscles, gut). The elimination half life for lidocaine (an amide) represents mainly hepatic metabolism, since renal excretion of unchanged drug accounts for less than 5 percent of the given dosage (Covino and Vassallo 1976).

2-6-3 METABOLISM OF LIDOCAINE

Lidocaine like other amide linked local anaesthetic drugs undergoes metabolic degradation in the liver by microsomal mixed function oxidases and amidases (Sung and Truant 1954, Hollunger, 1960, Backett et al, 1966).

It was demonstrated that the rate of disappearance of lidocaine from the blood of hepatectomized dogs was decreased. The same finding was demonstrated in two patients with terminal cirhossis undergoing liver transplantation. The finding was consistent with the hypothesis that the liver is responsible for the ultimate disposition of lidocaine (Adrete et al, 1970). Hepatic blood flow studies have shown that 70 percent of the injected dose of lidocaine is metabolized given the liver function is normal. If the latter is poor or completely absent, the breakdown of lidocaine is decreased resulting in elevated blood levels of which may result in toxicity (Stenson et al 1971). This has been evidenced by a case report of lidocaine induced central nervous system toxicity in a patient who had severe liver disease (Selden, Sasahara 1967).

There are several alternate metabolic pathways for the breakdown of lidocaine in man that have been uncovered. Some are minor while others are the major routes for the biotransformation. In the figure below, the major metabolic pathways for lidocaine breakdown in man are shown with solid arrows.

The biotransformation starts with the oxidative de-ethylation of diethyl-glycinexylidide (Lidocaine) yielding monoethyl-glycine xylidide (MEGX) and acetaldehyde. The MEGX is forther de-ethylated to glycine xylidide (GX). Oxidation of lidocaine and MEGX can also take place to yield meta-hydroxylidocaine (3-Hydroxylidocaine) and metahydroxy MEGX (3-Hydroxy MEGX) respectively. However this is unimportant as a biotransformation route in man. Then both MEGX and GX undergo hydrolysis to yield 2,6-xylidine which is hydroxylated in the para position to give 4-hydrocy-2,6-xylidine (para hydroxy-xylidine). Para hydroxy-xylidine accounts for 72.6% of all the urinary metabolites of lidocaine in man (Keenaghan and Boyes, 1972, Di Fazio and Brown 1971). Monoethylglycine xylidide (MEGX) retains much of lidocaine's cardiovascular activity and is comparable to lidocaine also in its potential to induce convulsions at elevated blood levels . Glycine xylidide (GX), of itself does not induce convulsions but given in conjunction with lidocaine or MEGX, potentiates their convulsant properties (de Jong 1977). Under normal physiological conditions, these metabolites exert relatively insignificant pharmacological or toxicological effects.

In certain situations such as renal or cardiac failure, or during prolonged periods of administration, these metabolites might accumulate and exert significant clinical effects (Covino and Vassallo 1976).

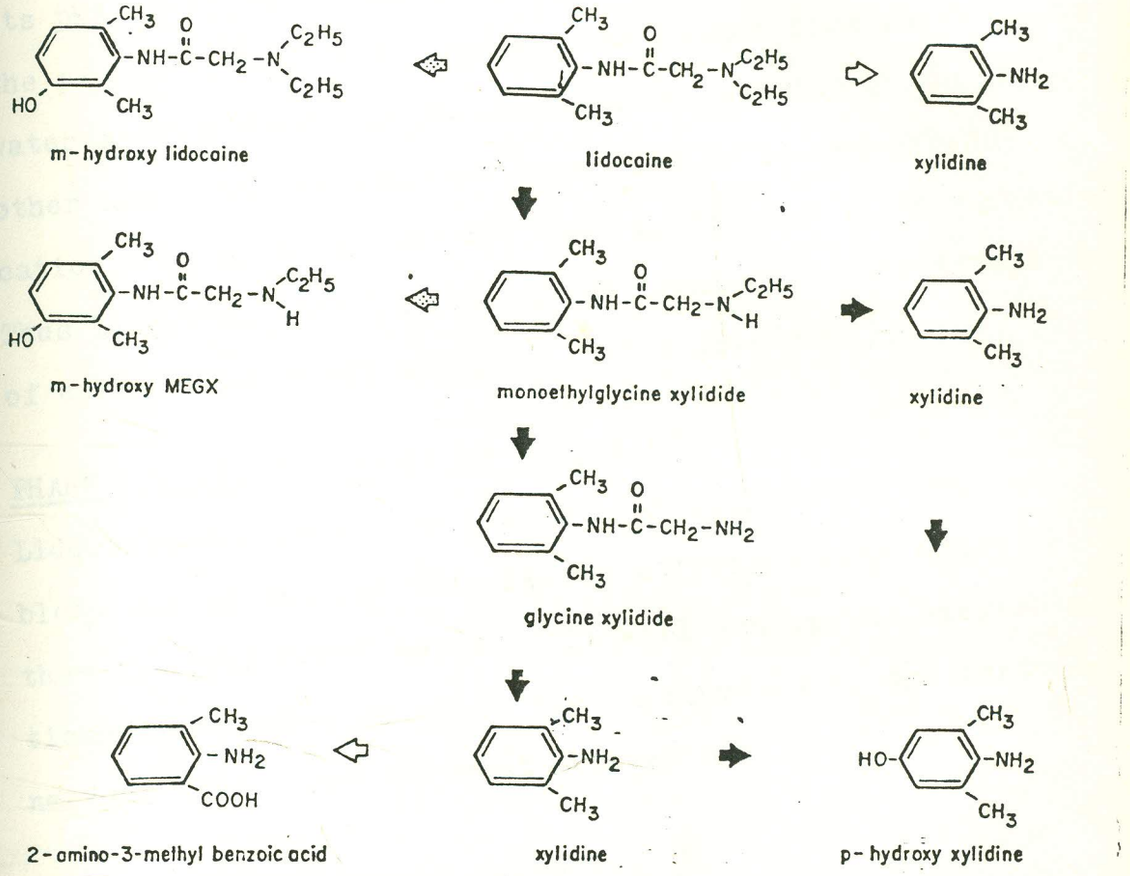

Fig. 9: Major Metabolic pathways for lidocaine in man are shown with solid arrows; minor routes indicated with stippled arrows point to products identified in other species, but not in man (de Jong 1977 pp 233).

2-6-4 EXCRETION

The kedney is the main excretory organ for lidocaine and its metabolites. Less than 10 per cent of intravenously given lidocaine was found in the urine of volunteers. About 80 percent of administered lidocaine could be recovered in human urine in the form of various metabolites (Keenaghan and Boyes 1972, Beckett et al 1966).

Impairment of renal function may thus result iniince increased blood levels of lidocaine or its metabolites which

The urinary excretion of lidocaine is pH-dependent because its pKa of 7.9 is close to the physiological pH. Lowering the pH will increase the protonated cation form which being water soluble tends to favour renal elimination. On the other hand, the metabolites like MEGX or GX are already cationic at urine pH and are thus unaffected by pH variations. Thus lidocaine elimination can be enhanced by acidification of urine in an event of toxicity (de Jong 1977).

2-7 PHARMACOLOGICAL EFFECTS OF LIDOCAINE

Lidocaine diffuses from its site of application into the blood stream and for this reason affects organs other than the peripheral nerves. It will act on any excitable tissue membranes, of which the cardiovascular and central nervous system are the most susceptible.

2-7-1 CENTRAL NERVOUS SYSTEM EFFECTS

Lidocaine in addition to its primary local effects on sensory and motor elements in the periphery, it induces a variety of central nervous system (CNS) reactions. These effects include sedation, central analgesic effects, psychotic reaction, anticonvulsant effect and convulsant effects (Selden and Sasahara 1967).

It has been demonstrated that intravenous lidocaine could produce both sedation and amnesia upon the central nervous system (Gilbert et al, 1951 and Steinhaus 1957). Central analgesic effects of lidocaine have been studied and six cases with intractable pain including carcinoma have been reported where opiates did not relieve pain but intravenous

lidocaine resulted in complete relief. (Gilbert et al 1951). However because of the systemic toxicity reactions it produces, lidocaine has not become popular as an analgesic by this route (de Jong 1977).

Lidocaine has also been used as an adjunct to general anaesthesia with successful results (Phillips et al 1960 Siebecker et al 1960). This method of conducting anaesthesia has not received wide acceptance, again because of the attendant risk of toxicity due to lidocaine.

Several workers have demonstrated the anticonvulsant action of lidocaine. Intravenous lidocaine was reported to be effective in aborting the seizures of status epilepticus (Benhard et al 1955). In support of Benhard et al, a controlled clinical trial confirmed that intravenous lidocaine was effective in aborting seizures of status epilepticus (Taverner and Bain 1958). They also established that lidocaine lengthened the interval between convulsions. It is thought that the mechanism of the anticonvulsant action of local anaesthetic agents in epileptic patients involves a depression of hyperexcitable cortical neurones (Covino and Vasallo 1976).

An isolated case of psychotic behaviour after local anaesthesia with lidocaine hydrochloride has been reported (Goldman 1958). However, this is a rare manifestation of central nervous system toxicity due to lidocaine. The Convulsant effect of lidocaine upon the CNS has been

demonstrated while comparing toxicity of intravenously given local anaesthetics in healthy volunteers (Foldes et al 1960). Both electroencephalographic and tonic-clonic convulsions have been demonstrated after intravenous administration of large doses of lidocaine in healthy human volunteers (Usubiaga et al 1966). Selden and Sasahara 1967, reported a case of generalized convulsions induced by lidocaine ina patient who had liver disease. In this case the elevated blood levels that led to the toxicity reaction were due to the diminished hepatic function to metabolize the drug. Further evidence on the convulsant action of lidocaine, noted when petit and grand mal convulsions were precipitated while using a course of lidocaine in the treatment of ventricular tachycardia (Crampton and Oriscello 1968).

At recommended clinical doses for regional anaesthesia, serum levels remain below the recognized toxic concentrations unless rapid absorption occurs due to inadvertent intravascular injection or due to injection in a highly vascular locale (Covino and Vassallo 1976). The early symptoms and signs of CNS toxicity include tinnitus, lightheadedness, visual and auditory disturbances, restlessness, garrulousness, slurred speech, nystagmus, shivering and muscular tremors. The EEG pattern during early toxicity is not diagnostic (Covino and Vassallo 1976, de Jong 1977). As dosage increases there is development of EEG Seizure activity with tonic-clonic convulsions. Finally these are followed by central nervous

system depression. The convulsive stage may be absent so that toxicity starts with CNS depression (Usubiaga et al 1966).

The CNS toxicity of lidocaine and other local anaesthetic drugs first starts with an excitatory phenomena which ends up just to be replaced by CNS depression. Toxic levels of the drug are thought to initially lead to depression of the cortical inhibitory pathways (de Jong et al 1969, Warnick et al 1971). This inhibition of the inhibitory pathways allows facilitatory neurons to function unopposed, leading to an increase in excitation of the CNS which is manifested as convulsive activity. As the dosage is increased further, both the inhibitory and facilitatory pathways are depressed thus ending in a generalized state of CNS depression (Wagman, de Jong and Prince 1966).

2-7-2 CARDIOVASCULAR EFFECTS OF LIDOCAINE

Lidocaine acts directly on the excitable, conducting and contracting elements of the heart. It also acts directly on the muscular wall of blood vessels. It acts indirectly by conduction blockade of autonomic nerve fibers that regulate cardiac and peripheral vascular functions (de Jong 1977, Covino and Vassallo 1976).

2-7-2-1 Cardiac Effects

Lidocaine has been used effectively and safely in the treatment of arrhythmias of ventricular origin (Harrison et al 1974, Rosen et al 1975). It has also been used as a prophylaxis against ventricular arrhythmias

in patients with acute myocardial infarction (Noneman and Rojer 1978, Ribner et al 1979, O'Brien et al 1975). Lidocaine however is not effective in supraventricular tachycardias. It is thus not used in atrial arrhythmias.

Electrophysiological Events:

These show a consistent sequence as the dose and subsequent blood levels are gradually increased. In the therapeutic dose range (i.e. non toxic but enough for antiarhythmic effect), lidocaine has the following effects on cardiac tissue:-

(i) Prolongation or abolition of phase of slow (spontaneous) depolarization during diastole (phase 4 depolarization in Purkinje fibers.

(ii) A shortening of action potential duration (APD)

(iii) A shortening of the effective refractory period (ERP).

(iv) Enhancement of conduction velocity at the Purkinje fiber ventricular muscle fiber junction.

While lidocaine slows spontaneous pacemaker depolarization (i.e. decreases pacemaker automaticity), the normal depolarization mechanisms are not changed by the normal dose range. There is no change in the resting membrane potential, rate of rise of action potential or (A-V) conduction and intra-ventricular (I-V) conduction. Normal therapeutic dose range of lidocaine slightly enhances conduction across the ventricular muscle - Purkinje junction. Bigger doses of lidocaine have the opposite effect of lowering

conduction velocity in the ventricular conducting system and increasing delay and refractoriness at the muscle-Purkinje junction (de Jong 1977).

As toxic doses of lidocaine are attained, there is a decrease in the maximum rate of depolarization of Purkinje fibers and ventricular muscle, a decrease in amplitude of the action potential and a reduction in conduction velocity. Except at extreme high doses of lidocaine the resting potential remains unchanged. The prolongation of conduction through various portions of the heart is reflected in the electrocardiogram as an increased PR interval and QRS duration and decreased automaticity as shown by sinus bradycardia. Finally, cardiac arrest (asystole) occurs with extremely high doses (Covino and Vassallo 1976)

Cardiac Contractility (Inotropy):

Therapeutic doses of lidocaine have minimal effects on the hearts contractility. When larger and larger doses are given, a dose-related decrease, in myocardial contractility (cardiac performance) occurs (Lieberman et al 1968). Various other workers have confirmed the direct negative inotropic action of toxic doses of lidocaine on cardiac muscle (Stewart et al, 1963, Nahas et al, 1969). Both atrial and ventricular contractility are depressed by the toxic doses of lidocaine (Richards, Smith and Katz, 1968). Thus a progressive increase in dose and blood levels results in decreased myocardial contractility, increased diastolic volume, decreased intraventricular

pressure and a decreased cardiac output all being indicators of decreased cardiac performance (Covino and Vassallo 1976).

Cardiac excitability:

Lidocaine produces a dose related rise in ventricular threshold to excitation. It also prevents spontaneous repetitive discharges following a premature stimulus. Partly this effect is secondary to the prolongation of the effective refractory period relative to the (shortened) action potential duration. Diazepam elevates the ventricular excitability threshold and its effect is synergistic with lidocaine (de Jong 1977). De Jong and Heavner 1973, suggest that diazepam given before lidocaine administration may enhance the latter's antiarrhythmic actions while at the same time reducing the likelibood of cerebral toxicity.

2-7-2-2 Blood Vessel Effects:

Lidocaine like other local anaesthetic agents have been shown to have a direct action on vascular Smooth muscle, since this effect can be reproduced both in innervated and denervated muscle preparations (Blair 1975). In their studies Jorfeldt et al 1970, showed that lidocaine at low doses produced an increased tone (stimulatory effect) of capacitance vessels with less consistent effects on resistance vessels. In other studies, it was shown that as the local anaesthetic dose was increased, there was an associated inhibition of myogenic activity in vitro and vasodilatation in vivo (Blair 1975, Nishmura et al 1965). In support of Blair and Nishimura studies, another study on man, showed that lidocaine caused vasodilatation

and an increase in forearm blood flow. (Dhuner and Lewis 1966).

The vasodilating doses of lidocaine include the therapeutically useful dose range, hence what we see clinically, are the peripheral vasodilating effects of lidocaine. Aberg and Anderson 1972, suggest that local anaesthetics relax smooth muscle of the blood vessels by blocking the excitation-contraction coupling mechanisms by interfering with Ca^{++} mobilisation.

2-7-3 RESPIRATORY EFFECTS OF LIDOCAINE

Keeping within the normal therapeutic dose range, lidocaine has minimal effects on respiratory function. Increasing the dosage to toxic blood levels, the drug can cause respiratory arrest due to its generalised central nervous system depressant action. Central neural blockade techniques (Epidural or Subarachnoid anaesthesia) may be associated with depression of pulmonary function tests. (Covino and Vassallo 1976). This is secondary to the involvement of the higher thoracic or cervical spinal nerve roots which innervate respiratory muscles. Sjogreen and Wright 1972, showed that a thoracic epidural anaesthesia extending from T_2- T_{12} produced a significant decrease in pulmonary function tests, but only minimal effects were noted following thoracolumbar epidural anaesthesia from T_4 - L_4. Ward et al 1965 demonstrated that a central neural blockade (Epidural and spinal anaesthesia) to the level of T_5 did not result in any deleterious change in blood gas tensions.

2-7-4 NEUROMUSCULAR JUNCTION EFFECTS

Lidocaine like other local anaesthetic drugs, impedes neuromuscular transmission. The precise mode of action of the drug is not exactly known however the neuromuscular blockade may involve pre-junctional, junctional or post-junctional structures. The neuromuscular blockade could be secondary to the drug acting simultaneously on all the three sites or effect at one site could be predominant (de Jong 1977). When clinically used, the neuromuscular blocking properties of lidocaine and other local anaesthetic drugs occurs only faintly. Significant blockade will be evident only when near toxic dosage levels are administered. While using subtoxic amounts of the local anaesthetic drug obvious meuromuscular blockade will occur only after intra-arterial administration of the drug (de Jong 1977).

Lidocaine prolongs and intensifies the respiratory paralysis produced by succinylcholine, but under the clinical setting this interaction is negligible (de Jong 1977).

2-7-5 UTERUS

Lidocaine and other local anaesthetic agents have minimal effect on myometrial contractions in blood levels met with during intrapartum regional anaesthesia. Blockade of the uterine nerves temporarily weakens and slows uterine contractions more so duri ng the early stages of labour. The effect wares as labour advances (de Jong 1977)

2-7-6 PERIPHERAL NERVOUS SYSTEM

Local anaesthetics negligibly affect axonal conduction or neuromuscular transmission even when given by the intravenous route. Only after intravascular anaesthetic concentration is further raised as by vascular isolation with a tourniquet is the minimum anaesthetic concentration (C_M) attained and impulse blockade achieved (deJong 1977).

2-7-7 OTHER PHARMACOLOGICAL EFFECTS OF LIDOCAINE

There are other pharmacological actions due to lidocaine and other local anaesthetics, these include anticholinergic activity (Wiedling1960) antihistaminic activity (Wiedling 1959), and bacteriostatic antimicrobial activity (Schmidt and Rosen Kranz 1970).

2-8 ADVERSE EFFECTS OF LOCAL ANAESTHETICS

Adverse effects due to local anaesthetic drugs may either be in the form of a localized reaction, a systemic reaction or a hypersensitivity (allergic) reaction (de Jong 1977).

2-8-1 Local Tissue (contact) Toxicity:

Localized reactions take place when the agent adversely affects the structures it contacts directly. Since a local anaesthetic drug is injected at concentrations several times higher than the theoretical minimum (to offset the inefficiencies of the delivery system) tissues in direct contact with this concentrated solution may be affected.

The nerve can be affected adversely by an overly long contact with an overly concentrated anaesthetic solution (de Jong 1977). However local anaesthetic agents in concentrations that are clinically available have not been shown to produce localized nerve damage (Benoit and Belt 1972). Most of the clinically used local anaesthetics such as lidocaine, mepivacaine, prilocaine, bupivacaine and etidocaine have been shown to cause histological changes in skeletal muscle. The more potent, longer-acting compounds appear to cause a greater degree of localized skeletal muscle damage than the less potent, shorter-acting agents. The effect is reversible and muscle regeneration is complete within two weeks after the injection of the local anaesthetic (Benoit and Belt 1972). However the skeletal muscle histological changes are not associated with any overt clinical signs of irritation. It has been demonstrated that there is an elevation of blood creatine phosphokinase (CPK) levels, following intramuscular administration of lidocaine which is suggestive of skeletal muscle damage (Zener and Harrison 1974).

2-8-2 Systemic Toxicity:

In systemic toxicity the local anaesthetic agent is blood borne thus enabling it to reach and cause effect at distant organs. The systemic reactions are dose dependent, that is, the higher the anaesthetic concentration in the blood, the more pronounced the response (de Jong 1977).

Local anaesthetic toxicity involves mainly the central nervous system (CNS) and the cardiovascular system (CVS). A high local anaesthetic blood level causing toxicity reactions is achieved either by a rapid inadvertent intravenous injection or administration into a highly vascular locale or administration of an excessively large dose of the local anaesthetic drug. The sequence of events in systemic local anaesthetic toxicity is as follows:-

(a) Premonitory CNS symptoms - These include dizziness, ringing in the ears (tinnitus), vague sensation of light headadness, nystagmus, and fine skeletal muscle twitching of face and digits.

(b) Then follows overt seizure activity (convulsions) of a clonic and tonic nature. After which follows

(c) CNS depression in which seizure activity terminates and respiratory efforts become shallow, and ultimately cease.

(d) There is a fall in systemic blood pressure and

(e) a progressive bradycardia leading ultimately to cardiac arrest. Sometimes rapid achievement of an extremely high anaesthetic blood level may produce respiratory depression and cardiovascular collapse without the usual signs and symptoms of CNS excitation (Covino and Vassallo 1976).

2-8-3 Allergic Reactions

Allergy is an adverse reaction to a local anaesthetic drug resulting from previous sensitization to that same compound or a closely related one. An allergic reaction unlike systemic toxicity is not linked to the drug mass. A minute dose of a drug is sufficient to trigger off a massive

off a massive allergic response (de Jong 1977).

Allergic drug reactions due to local anaesthetics are quite rare as has been noted from the many instances in which they are used daily in clinical anaesthesia (Moore 1966) (Collins 1966). Most reports of local anaesthetic drug allergy indicate that esters of para-aminobenzoic acid such as procaine, tetracaine, chloroprocaine or benzocaine, are the ones responsible for such adverse reactions. Allergy due to amide type drugs such as lidocaine, mepivacaine, bupivacaine or etidocaine is extremely rare (Aldrete and Johnson 1969). Patients subjected to skin testing for possible allergy to local anaesthetics responded only to the ester-type compounds whereas no skin reaction at all was noted after intracutaneously administered amide local anaesthetics (Aldrete and Johnson 1970). Solutions of amide -type local anaesthetic agents may contain methylparaben as a preservative. Methylparaben has a structure similar to para-aminobenzoic acid. Some patients who were thought to be allergic to lidocaine have shown a positive skin response to methylparaben, but not to lidocaine itself (Aldrete and Johnson 1969).

Allergic reactions when they occur, manifest as generalized erythema, oedema, respiratory wheezing and/or dyspnoea, hypotension, tachycardia, headache, or loss of consciousness (all symptoms of histamine release and all occurring within only a few minutes of local anaesthetic administration (Covino and Vassallo 1976).

2-8-4: MANAGEMENT OF ADVERSE EFFECTS

The first step in the management of adverse effects due to local anaesthetic drugs involves the prevention of these effects from occuring.

Preventive measures include the following:-

i) A thorough knowledge of the pharmacologic characteristics of the drug used is mandatory before any attempt of applying it in a procedure is planned.

ii) The drug dosage should be limited to the smallest amount necessary for the performance of the procedure in order to avoid toxicity.

iii) A careful technique coupled with frequent aspiration testing as the drug is injected will prevent an inadvertent intravenous injection from occurring.

iv) Avoidance of drugs which the patient is known to be allergic to, will prevent hypersensitivity reactions from taking place.

v) Premedication with a benzodiazepine such as diazepam 0.1 - 0.2mg/kg provides prophylaxis against CNS toxic effects due to local anaesthetics (de Jong and Heavner, 1971, Munson and Wagman 1972, Ausinsch et al 1976).

Treatment Measures:

Treatment of local anaesthetic toxicity is both supportive and therapeutic. The first and foremost supportive measure is the maintainance of the airway with administration of oxygen by assisted or controlled ventilation. Bronchodilator therapy may be mandatory in cases of a severe hypersensitivity reaction manifesting with bronchospasm. Circulatory support is achieved by proper

positioning of the patient (the Trendelenburg position), intravenous fluids through a large bore canula and vasopressor drugs such as ephedrine. In cases of severe allergic reaction, antihistamines and corticosteroids may be necessary to control the physiological effect of systemic histamine release. Mild CNS reactions are usually abated by giving oxygen alone. With more severe CNS signs as manifested by marked CNS excitation or frank seizure activity an anticonvulsant drug such as diazepam (0.05mg - 0.1mg 1kg) or thiopentone sodium 1 to 2mg/kg is given. While using thiopentone care should be taken that only small doses are given in order to avoid respiratory and cerebral depression that may ensue. A short acting neuromuscular blocking agent like succinylcholine 0.5 - 1mg/kg has been recommended to avert the muscular manifestation of the seizure. The muscular paralysis that follows will also facilitate intubation of the airway and hence enable better ventilation (de Jong 1977).

2 - 9 THE CLINICAL USES OF LIDOCAINE

Lidocaine is used for various procedures in surgical anaesthesia and has also got some therapeutic application in some medical conditions. The maximal safe dose is 300mg (3mg/kg) when given without adrenaline and 500mg (7mg/kg) when mixed with adrenaline. A summary of the clinical uses of lidocaine is given below.

1. Infiltration Anaesthesia

For extravascular infiltration anaesthesia 0.5 - 1% solutions are used. A 2% lidocaine with adrenaline 1:200,000 has been used to attain gingival anaesthesia in dentistry.

For intravascular infiltration (i.e. Intravenous regional anaesthesia or Bier's block) a 0.25 - 0.5% lidocaine solution is used. Dose range varies from 1.5mg/kg to 3mg/kg. For the upper extremity a dose of 3mg/kg as a 0.5% solutions is used. Most adults will thus need 40 - 50ml of solution (Holmes 1963). If a pre-injection period of ischaemia is used, then a smaller volume may be used on the basis of a dose of 1.5mg/kg or a volume of 20 - 24ml of a 0.5% solution is injected (Adams et al 1974). For the lower extremity the dose is also 3.0 mg/kg but a solution of 0.25% is used hence the volume is doubled.

2. Peripheral Nerve Blockade

Lidocaine is used to attain minor nerve blockade (i.e. single nerve block) and major nerve blockade (i.e. multiple nerve blockade or plexus blockade) as a 1% 1.5% or 2% solution with or without adrenaline 1:200,000.

3. Sub-arachnoid Block (Spinal Anaesthesia

A hyperbaric solution of lidocaine (5% lidocaine solution with 7.5% Dextrose) is used to achieve subarachnoid blockade.

4. Epidural Block

For epidural anaesthesia a 1-2% lidocaine solution with or without adrenaline 1:200,000 is used.

5. Topical Anaesthesia

To attain surface anaesthesia various lidocaine concentrations in the form of solution, jelly, aerosol or ointment are used.

i) 2 - 4% lidocaine solution is used for application to the cornea, pharynx, larynx and the tracheobronchial tree.

ii) A 2% jelly preparation is used for urethral endoscopy and on endotracheal tubes.

iii) A 10% aerosol preparation is used on the perineum and vagina in obstetrics, during spontaneous delivery or for suture of simple lacerations.

iv) A 2.5% - 5% ointment is available for skin preparation.

6. Adjunct to general Anaesthesia

Lidocaine is used as a supplement to general anaesthesia. This is based on the fact that lidocaine produces central sedative analgesic effect when introduced into the blood stream in appropriate doses. A peripheral tissue effect is also present which in part accounts for the suppression of reflexes (Collins, V.J. 1976).

7. Anticonvulsant

Most of the clinically useful local anaesthetic agents have been demonstrated to have inherent anticonvulsant activity. Lidocaine has been used to prevent and/or reduce the duration of electrically induced seizures in patients (Wikinski et al 1970). Lidocaine has also been utilized to terminate or decrease the duration of grandmal or petitmal seizures (Benhard and Bohm 1965). The mechanism of the anticonvulsant action of local anaesthetic agents in epileptic patients probably involves the depression of hyperexcitable cortical neurons (Covino and Vassalo 1977).

8. Therapy of Arrhythmias

Lidocaine given intravenously decreases the ventricular irritability, and the diastolic threshold of the myocardial muscle fiber is elevated. There is no depressant action on the cardiac output and peripheral vascular system. Lidocaine is not effective in supraventricular arrhythmias and in arrhythmias due to digitalis overdose (Collins 1976). The clinical indications for intravenous lidocaine for this purpose are the following:-

i) Suppression of ventricular irritability during cardiac surgery.

ii) Reduction of cardiac irritability due to hydrocarbon anaesthetics.

iii) Control of arrhythmias related to cardiac arrest, especially ventricular fibrillation.

iv) For management of cardiac arrhythmias in patients with coronary artery disease, and for coronary occlusion or myocardial infarction.

v) Prophylactic use in myocardial infarction.

PART 3

CLINICAL STUDY

BRACHIAL PLEXUS BLOCKADE BY LIDOCAINE ONE PERCENT WITH ADRENALINE 1:200,000 FOR UPPER LIMB SURGERY.

PART 3: CLINICAL STUDY

3 - 1 INTRODUCTION

A study of brachial plexus blockade for operations on the upper limb using lidocaine one percent with adrenaline 1:200,000 solution was done over a one year period. The study population included both emergency and elective operations. The brachial plexus blockade was effected by two approaches, the supraclavicular and the axillary approach. For each approach of brachial plexus blockade, it was aimed to study on the success rate, nature and incidence of complications, latency of analgesia and the duration of analgesia. The study was also aimed at comparing the two approaches in terms of success rate of block, incidence of complications, onset of analgesia (latency) and the duration of analgesia.

3 - 2 PATIENT AND METHOD

Patients

The study included patients who presented to the anaesthesiology department for surgical operation or manipulation of the upper limb. Patients studied were admitted either for elective or emergency operations. There were 40 randomly selected patients in the study group. For each case, a prior discussion with the operating surgeon was made on the approximate duration of surgery. Duration of surgery ranged from 30 minutes to 150 minutes. Any case with an anticipated prolonged duration of surgery was not included in the study. Patients with multiple injuries were also not included in the study population.

The ASA physical status of the patients in the study population varied from ASAI to ASA IV classification. The patients were divided in two equal groups, I and II. There were 20 patients in group I and for these a supraclavicular approach to brachial plexus blockade was done. In these surgery performed was either above or below the elbow depending on the surgical problem. In group II there were also 20 patients and in these brachial plexus blockade was achieved by the axillary approach. Group II included only patients who had operation done below the elbow level.

Patients presenting with surgical problems of the upper limb and in whom surgery was planned, were requested to undergo brachial plexus anaesthesia after it had been clearly explained to them. Those who opted for general anaesthesia were not denied their choice and as such they were not included in the study. Those patients who accepted the local anaesthetic method had the procedure explained to them both at the pre-operative visit and immediately before the procedure. The need for cooperation when paraesthesia was elicited was emphasized.

Materials

Lidocaine 1% (xylocaine, Lignocaine) was freshly mixed with adrenaline 1:1000 solution. The adrenaline dilution was 1:200,000 in the local anaesthetic solution. This mixture was achieved by introducing 0.1ml of a 1:1000 solution of adrenaline to each 20ml of Lidocaine solution using a tuberculin syringe. A 20-cc syringe

was used for the injection. A 23 - gauge 3.8 c m needle with a short bevel was used for the supraclavicular approach while a 23-gauge 2.5cm needle with a short bevel was used for the axillary approach. A short bevelled needle (Sherwood B 400 27G/short) was used to assess analgesia after the blockade procedure. A dilute iodine solution (1%) was used to effect antisepsis on the injection site.

Estimation of the dose of the local anaesthetic required to effect a brachial plexus blockade was done according to the rule given by Winnie 1975. By this rule, half of the patients height in inches indicates approximately the proper volume of anaesthetic required in millilitres. In the present series, between 26.5ml - 35.5ml of lidocaine were used for each procedure. During the performance of each procedure, resuscitation equipment and drugs were ever present.

Anaesthetic Procedure

Elective operation cases were fasted and prepared as for a general anaesthetic. These were given lomg of diazepam orally the night before operation. Diazepam 10mg was given orally 1-2 hours before the blockade procedure, as a premedication. Patients received as emergencies were not premedicated. Every patient had an intravenous canula placed in the dorsum of the contra-lateral hand before commencement of the blockade procedure. After the procedure, the patients were followed up for 24 hours.

Group I: The Supraclavicular Approach

The patient was made to lie supine on the operating table with the head on a shallow pillow and arms on the sides. The face was turned to the side opposite that being anaesthetized. The shoulder and arm of the affected side were depressed by requesting the patient to reach with the tips of his fingers down the lateral aspect of the ipsilateral leg. The supraclavicular area was swabbed with a 1% iodine solution and then draped with sterile drapes.

The clavicular head of the sternomastoid muscle was identified and the subclavian artery was located by palpation just lateral to the sternocleidomastoid muscle. The midpoint of the clavicle was identified. Through a raised intradermal wheal, a 23-gauge 3.8cm needle was inserted 1cm above the midpoint of the clavicle (immediately lateral to the subclavian artery). The needle was advanced slowly backward, inward and downward to the first rib. The index finger of the anaesthesiologist's opposite hand was feeling for and protecting the subclavian artery by pressing it medially. When paraesthesias to the forearm and fingers were elicited, the needle was steadied and an aspiration test done if negative, all of the estimated local anaesthetic solution was injected. If paraesthesias were not elicited in the process of advancing the needle towards the first rib, then the first rib was contacted and the needle was walked along the rib in anteroposterior directions. This was done until paraesthesias were elicited, when the

needle was steadied and an aspiration test done. If negative, the estimated dose of the lidocaine solution was injected, care being taken not to move the needle.

Group II - The Axillary Approach:

The patient was made to lie supine on an operation table. The limb being anaesthetized was abducted to 90 degrees the forearm being flexed at the elbow and the hand placed under the head. In most cases, due to trauma pain or limb deformity which could not allow this abduction and flexion, the blockade had to be done in a position less than the ideal one. A tourniquet (Penrose drain) was applied tightly on the arm distal to the point of injection; this prevents spread of the anaesthetic solution peripherally. The tourniquet was removed 5 - 10 minutes following completion of the block. The axillary area and shoulder areas were swabbed with an antiseptic solution (1% iodine solution) and draped with sterile drapes.

The axillary artery was palpated as high as possible in the axilla and was then fixed against the humerus by the anaesthesiologists index finger. A skin wheal was raised and a 23-gauge, 2.5cm needle was inserted until a click was felt as the axillary sheath was penetrated, and the pulsations of the axillary artery were transmitted to the needle. The correct placement of the needle within the neurovascular bundle was verified either by paraesthesias radiating down the arm to the fingers or aspiration of blood into the syringe. If paraesthesias are obtained, the estimated volume of 1% lidocaine solution was administered after a negative aspiration test. If

blood was aspirated, the needle was withdrawn until the aspirationof blood was negative, and then the estimated anaesthetic solution volume was administered. In this series a relatively large volume of 30 - 35ml of 1% lidocaine with adrenaline 1:200,000 was used.

Measured Parameters

During the procedure the usual vital parameter monitoring was done. Pulse and Blood Pressure monitoring was done immediately after the completion of injection and then every 5 minutes for the first 15 minutes. Thereafter these two vital parameters were recorded ¼ hourly until completion of the operation.

1. Latency (onset) of Analgesia - This parameter was observed according to the description given by Bromage and Gertel 1972. Latency of analgesia was taken as the time lapse from the commencement of the injection to development of complete analgesia in all cutaneous areas of the hand and forearm. This was decided upon by reaction to pin-prick done by 27G short bevel needle every 5 minutes after completion of block until there was complete analgesia. If analgesia was not achieved in 30 minutes, the procedure was abandoned.

2. Gradation of Block Effect

   The success of the blockade was graded and recorded as follows:

   Grade A - This was when there was complete analgesia achieved after the block.

Grade B - This was a satisfactory block. That is when the block performed allows the patient to tolerate a surgical procedure despite some restlessness OR when a supplementary analgesic or sedative was all that was required to induce calm to the patient.

Grade C - Failed block. This is when there was incomplete analgesia or no analgesia at all, such that the patient needed a re-block or change to general anaesthesia.

Grades A and B were regarded as successful blocks in the present study.

This gradation method is closely similar to that used by Ward 1974, inhis study of brachial plexus blockade by the interscalene approach. In his study he grades analgesia after block in grades 1 to 5. In the present study Grade A is equivalent to Grade 1 by the Ward's method, and Grade B is equivalent to grades 2 and 3. Grade C represents grades 4 and 5 by Ward's method.

3. Complications - All complications whether due to the adverse effect of the drug used or the procedure itself were noted and recorded. Patients were followed up for 24 hours post block to look for the development or persistence of unfavourable sequelae due to the block.

4. Duration of Analgesia - This parameter was rated according to the description in the paper by Bromage and Gertel 1972. Duration of analgesia was taken as the time from complete development of analgesia until the first return of pin-prick sensation in any cutaneous area of the hand or forearm,, or to the first awareness of pain, whichever occurred sooner. Persistence or absence of analgesia was tested for by reaction to pin-prick and by asking the patient about awareness of pain every 15 minutes after onset of complete analgesia.

3 - 3 RESULTS

The study group consisted of 40 patients divided into two groups. Twenty patients underwent a supraclavicular technique blockade of the brachial plexus and on the remaining 20, an axillary technique blockade was performed. These were labelled as group I and II respectively.

There were 27 males and 13 females in the study group. The preponderance of males could be explained by the more frequent involvement of males in physical activities with the attendant risk of trauma to the upper limb.

Table 1: Frequency Table for Sex Distribution

Sex	Group I	Group II	Total	%
Male	14	13	27	67.5
Female	6	7	13	32.5
Total	20	20	40	100.0

Preliminary data of Age, Weight and Height was recorded for each patient. The ranges and means for each of these variables appear in tables II, III and IV respectively. The mean age was 32.9 years while the range in years was between 14 - 68 in Group I patients. For Group II patients the mean age was 28.5 years and the range was 16 - 45 years. The two groups were comparable. There is a young age group preponderance, this again could be due to the more physically active life style in this age group leading to the increased chances of trauma.

The mean height in inches was 62" with a range of 53" - 71" for group I patients and a mean of 63" with a range of 60" - 70.4" in group II patients.

The mean weight and range was 59kg and 30 - 80.7kg respectively for group I patients. For group II patients the mean weight and range were 58.2kg and 44.4 - 66.0kg respectively.

TABLE II: Mean Age and Range

Age (YR)	Group I	Group II
Mean	32.9	28.5
Range	14-68	16-45

TABLE III: Mean Height and Range

Height (Inch)	Group I	Group II
Mean	62"	63"
Range	53" - 71"	60-70.4"

TABLE IV: Mean Weight and Range

Weight (Kg)	Group I	Group II
Mean	59.0	58.2
Range	30-80	44.4-66.0

Grades of Blockade

Grades A and B were regarded as successful blocks. There were in total 35 successful blocks and these made 87.5 percent of all the cases.

TABLE V: Frequency Table for Blockade outcome.

Grade of Block	Frequency	%
C	5	12.5
B	12	30.0
A	23	57.5
TOTAL	40	100.0

Complications

There were more complications after the supraclavicular technique (15%) than after the axillary technique (5%) for brachial plexus blockade. The complications in Group I included two cases of haematoma formation. These haematomata, were however not serious and had resolved completely after 24 hours. The other complication was a Horner's

syndrome due to incidental stellate ganglion blockade. This was not a serious complication. In group II there was one complication and this was a haematoma which resolved in 24 hours.

TABLE VI: Frequency Table for Complications by Technique

Technique	Frequency	Total	%
Supraclavicular	3	20	15
Axillary	1	20	5
Total	4	40	10

Grade of Block by Technique

There was a 90% success rate of blockade by the axillary route (i.e. group II) while it was 85% successful by the supraclavicular technique (Group I). Grades A and B were regarded as successful.

TABLE VII: Frequency Table for Outcome by Technique

Technique	A	B	C	(A+B)	Total	(A+B)%
Supraclavicular	10	7	3	17	20	85
Axillary	13	5	2	18	20	90

Onset of Analgesia (Latency)

The average latency (onset time) for the supraclavicular technique was 13.99 $\pm$ 2.49 minutes while it was 14.92 $\pm$ 2.59 minutes for the axillary approach. The ranges were

9.50 - 19.0 minutes and 10.50 - 21.50 minutes respectively. The mean latency was similar in the two techniques.

TABLE VIII: Onset of Analgesia and Range (in minutes)

Technique	Range (Min.)	Mean ± S.D.
Supraclavicular	9.5-19.0	13.99 ± 2.49
Axillary	10.5-21.5	14.99 ± 2.59

Duration of Analgesia

The mean duration of analgesia while using the supraclavicular method was 166.5 ± 37.7 minutes with a range of 126 - 230 minutes. By the axillary route the mean duration of analgesia was 167.7 ± 33.2 minutes with a range of 127 - 227 minutes. There was no difference in the mean duration of analgesia between the two approaches to the brachial plexus block.

TABLE IX: Duration of Analgesia

Technique	Range (min)	Mean duration + S.D.
Supracla-vicular	126 - 230	166.5 ± 37.7
Axillary	127 - 227	167.7 ± 33.2

3 - 4 DISCUSSION

The study presents 40 patients for manipulation or surgical operation of the upper limb by applying brachial plexus blockade anaesthesia. Of the forty patients, 87.5% had successful blocks that enabled surgical procedures to be performed. The remaining 12.5% were graded as blockade failures and resort to general anaesthesia had to be done. For the 20 patients in Group I i.e. those in whom brachial plexus block was achieved through the supraclavicular approach, there was an 85% success rate. Brand and Papper 1961, while using lidocaine 1% with adrenaline, reported a success rate of 84.4% in their series of 194 patients for the supra-clavicular block. This finding does compare well with our present series. Before adoption of lidocaine in clinical anaesthesia, Murphey 1944 did a supraclavicular brachial plexus blockade using procaine 2% with adrenaline, and got a success rate of 93.4% in his series of 45 patients. The three different studies do compare well and it seems a different local anaesthetic used does not vary the outcome of blockade success.

By the supraclavicular approach there were 3 cases (15%) in whom the blockade failed and resort to general anaesthesia had to be done.

The first failed block was in a patient scheduled for open reduction and fixation due to a supra-condylar fracture of the left arm. This patient was a very obese man. He received 35.5ml of the lidocaine solution and 30 minutes post block there was no analgesia produced in the limb. General anaesthesia was thus induced by thiopentone and maintained by nitrous oxide, oxygen and halothane. The second blockade failure was in a fat female patient scheduled for closed reduction and plaster of paris casting due to a fracture of the right humerus. In this patient 35.5ml of lidocaine 1% with adrenaline were injected. In this case, there was incomplete analgesia of the upper limb and as such the patient could not tolerate surgery and resort to general anaesthesia by a single dose ketamine intramuscularly was applied. The third case of failure was in a 16 year old boy who had come for release of right elbow contracture. This patient was apprehensive and was uncooperative during the procedure. 30.5ml of Lidocaine 1% with adrenaline, were injected supraclavicularly without attainment of analgesia in the upper limb. A resort to general anaesthesia was done. Thiopentone induction followed by suxamethonium intubation and maintenance by nitrous oxide, oxygen and halothane was done.

Failure to obtain anaesthesia in the above cases can be due to various reasons. An inactive local anaesthetic solution could account for a failed block. But this could not explain blockade failures in this series since the lidocaine solution was freshly mixed with adrenaline and was of undisputable potency because the same batch of the agent had worked excellently in other blocks. Failure to inject the lidocaine solution in contact with the plexus could be a possible alternative explanation to blockade failure. In the first case of blockade failure, there was some difficulty in eliciting paraesthesias due to the gross obesity of the patient. There was a high chance of depositing the anaesthetic far from the plexus. This could explain the blockade failure. For the second failure, which got an incomplete analgesia, paraesthesias were elicited without difficulty and in this case the blockade failure could not be accounted for. The last blockade failure could also not be accounted for, since the correct needle placement had been verified by elicitation of paraesthesias.

In the 20 patients (Group II) who got brachial plexus blockade by the axillary approach there was a 90% success rate. De Jong 1961, in his series of 94 axillary blockades by 1% lidocaine with adrenaline reports a success rate of 91.5%. Brand and Papper 1961 also reported a 91.5% success rate. The results

from these two studies do compare closely with the present series. There were two blockade failures (10%) by the axillary approach to brachial plexus blockade. The first was in a 28 year old man scheduled for closed reduction and Plaster of Paris cast due to fracture radius and ulna of the left side. 30ml of lidocaine 1% with adrenaline were injected into the axillary sheath by the technique described above, without achievement of analgesia. Correct placement of the needle within the sheath was proven by axillary artery blood aspiration. The second failed axillary block was in a 35 year old man who was to undergo surgical toilet and Plaster of Paris cast due to a compound fracture left radius. A volume of 31.5ml of lidocaine 1% with adrenaline were injected into the axillary sheath after elicitation of paraesthesia. There was no clear reasons to explain these two failed blocks.

In the present series between the two approaches to brachial plexus blockade the axillary approach carried a higher success rate (90.0%) than the supra-clavicular one (85%). This observation is similar to that by Brand and Papper 1961, who reported a higher success rate by the axillary approach (91.5%) than by the supraclavicular approach (84.4%). The needle's small diameter makes perforation of a vein or artery incosequential (de Jong 1961). In our series a 23-G short bevel needle was used, hence resulting in less bleeding and haematoma formation in our series.

The overall incidence of complications was higher in the supraclavicular block group (15%) than in the axillary block group (5%). Despite the small study population in our series, a similar pattern was reported in the paper by Brand and Papper 1961 in which the incidence of complications by the supraclavicular route was 9.1% while it was 2% by the axillary route.

The most dreaded hazard associated with the supraclavicular approach to brachial plexus blockade is of penetration of the dome of the pleura and lung apex resulting in pneumothorax. De Jong 1961 reports an incidence of pneumothorax of 2.5% when this route is used, while Moore 1965 reports an incidence of between 0.5 and 4%. However this complication was not found in any of our 20 patient series. The absence of this complication could possibly be accounted for by the small 23 G needle used in the series. A microperforation caused by such a needle could possibly not result in clinically evident pneumothorax. No patient complained of symptoms or had signs suggestive of pneumothorax.

Other than the Horner's Syndrome reported, there was no other temporary or permanent postoperative neurological sequelae encountered in our present study. Other studies by Selander et al 1977, Selander et al 1979, have reported neurological sequelae post brachial plexus blockade. In our

series a small 23 - G needle with a short blunt bevel was used. The blunt bevel displaces the nerves and thus makes injury to the nerves a remote possibility (Selander et al 1977).

There were no signs of local tissue irritation, systemic toxicity or depression of the central nervous or cardiovascular systems encountered in the present study, despite the ever present risk of intravascular injection.

In this study the analgesia onset time for Group I (The Supraclavicular approach group) averaged 13.99 ± 2.49 minutes. While using lidocaine 1% with adrenaline, for supraclavicular brachial plexus blockade, Bromage and Gertel 1972, found a mean onset time of 14.07 ± 3.76 minutes. Their finding closely compares with that of our present series. For Group II (axillary approach group) the mean analgesia onset time was 14.92 ± 2.59 minutes. In his paper on axillary block of the brachial plexus, de Jong 1961, reports a mean onset time of 15 minutes. This compares with the results in the present series. From this study, it is evident that the mean analgesia onset time in the two groups do not differ, being 13.99 ± 2.49 and 14.92 ± 2.59 minutes for the supraclavicular and axillary approach respectively.

With regard to onset of action, lidocaine has been found to possess a significantly shorter latency than buvacaine for peripheral nerve blockade.

Bromage and Gertel 1970, observed a mean onset time of 14.04 ± 3.83 minutes for 1% lidocaine with adrenaline 1:200,000 when used for brachial plexus blockade as compared to an average onset time of 23.26 ± 7.93 minutes for 0.25% bupivacaine with adrenaline. Etidocaine (Duranest) a newer, potent and longer acting local anaesthetic drug has also been used to attain brachial plexus anaesthesia. Etidocaine has a more rapid onset of analgesia than lidocaine. Lund et al 1974, while using etidocaine 0.5% with adrenaline 1:200,000 for brachial plexus block found an average onset time of 9.0 ± 3.4 minutes. Being a potent and long acting drug, etidocaine would be ideal for brachial plexus blockades where a rapid onset of action and prolonged analgesia were required.

Mepivacaine (carbocain) can also be used for brachial plexus block anaesthesia. It is similar to lidocaine in terms of potency, onset of analgesia and duration of analgesia (Covino 1976).

The slow analgesic onset time that characterizes the brachial plexus blockade is one of the deterrents to the popular use of this method in upper limb surgery. Attempts to circumvent this shortcoming have been suggested by the use of carbonated salts of local anaesthetics instead of the hydrochloride salts. The carbondioxide salts have a shorter analgesic onset time. Bromage and Gertel 1972,

reported a reduction in the onset time of brachial plexus blockade from a mean of 14 minutes with lidocaine hydrochloride to 8 minutes with carbonated lidocaine. The solution used in the present series was a hydrochloride salt.

In the present study a solution of lidocaine 1% with adrenaline 1:200,000 was freshly prepared and used. Adrenaline was used for its vasoconstrictive properties. In general, it is believed vasoconstrictors tend to prolong the duration of action of local anaesthetic agents and reduce the potential toxicity of these compounds by decreasing the rate of absorption from the site of injection. Addition of adrenaline to lidocaine prolongs the duration of action and reduces the rate of absorption of this agent (Bromage, 1962; Scott et al, 1972).

Most of the operations in the study population lasted from between 30 minutes and 2½ hours. There was no occasion when the duration of operation outlived the duration of analgesia. The average duration of analgesia by the supraclavicular approach (Group I) was 166.5 ± 37.7 minutes, varying from 126 to 230 minutes. Bromage and Gertel 1972, using lidocaine 1% with adrenaline 1:200,000 for brachial plexus blockade, reported a mean duration of analgesia of 196 minutes with a range of 140 - 235 minutes. These results compare well with those of the present series.

The mean duration of analgesia in the two methods of brachial plexus blockade showed no difference. It was 166.5 + _ 37.7 and 167.7 ± 33.2 minutes for the supraclavicular and axillary approach respectively. Covino and Vassallo 1976, give an average duration of analgesia for brachial plexus blockade as being 195 - 245 minutes, when lidocaine 1% with adrenaline is used. This compares well with the results in the present study. The potent and long acting local anaesthetic agents Bupivacaine (Marcaine) and Etidocaine (Duranest) have relatively longer durations of action when used for brachial plexus blockade. Bromage and Gertel 1970, while using bupivacaine 0.25% with adrenaline 1:200,000 to achieve brachial plexus blockade, reported a mean duration of sensory analgesia of 613.0 ± 126 minutes. The duration of action of bupivacaine was found to be approximately 300% greater than that of lidocaine (Bromage and Gertel 1970).

Etidocaine in concentrations of 0.5% to 0.75% with adrenaline when used for brachial plexus blockade was found to have a duration of action ranging from 10 to 15 hours (Lund et al 1974). This agent is the longest acting of the presently known local anaesthetic drugs.

The potent and long acting anaesthetic agents would be of use in brachial plexus blockade. Etidocaine particularly because of its rapid onset of action

combined with its prolonged duration increases indications for conduction anaesthesia in cases where a long duration of surgery is anticipated (Lund et al 1974). In the present series with lidocaine, those cases where prolonged surgery was anticipated were not included in the study population. When long acting drugs are used, the ensuing prolonged numbness and immobilization of the upper limb following brachial plexus block for a simple operation like a closed reduction may be upsetting to the patient even though it is accompanied by prolonged freedom from pain.

In one case in group I, a tourniquet was applied on the upper arm, while corrective osteotomy for distal third malunion of radius and ulna was being done. After brachial plexus blockade by the supraclavicular route, a half-ring subcutaneous local infiltration with 1oml of lidocaine was done in the axilla, before the tourniquet was applied. This manouvre anaesthetizes the intercosto-brachial (T_2) nerve and the medial brachial cutaneous (T_1, T_2) nerves which innervate the medial and inner surfaces of the arm. This procedure enabled the tourniquet to be tolerated without pain being felt.

3 - 5 SUMMARY

The present study evidently shows that brachial plexus blockade can successfully be applied to achieve anaesthesia for upper limb surgery in 87.5% of the cases. The axillary approach to brachial plexus blockade had a higher success rate than the supraclavicular one. Furthermore, the axillary approach was associated with a lower incidence of complications than the supraclavicular one.

The mean onset of analgesia (latency) and the mean duration of analgesia was comparable in both approaches to brachial plexus blockade. It is thus advisable to use the brachial plexus blockade for upper limb surgery and where indicated the axillary route should be the method of choice.

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