COMPARATIVE QUALITIES OF THREE NEW LOCAL ANESTHETIC DRUGS: XYLOCAINE®,* CYCLAINE®,† AND PRAVOCAINE® ‡

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ALTHOUGH there are a number of factors which might advance the over-all acceptance of regional anesthesia, there is one outstanding need from the viewpoint of the anesthesiologist; the introduction of a local anesthetic drug with a wide clinical utility and an over-all efficiency superior to existing drugs. The problems of toxicity, slow onset of anesthesia, poor diffusion qualities, instability, low activity, lack of clinical utility, and so forth have created a barrier to the anesthesiologist in selecting a regional block rather than inhalation or intravenous anesthesia. Research has provided us with innumerable local anesthetic drugs, which have undergone various degrees of clinical investigation in an effort to provide a universally accepted drug. It is the purpose of this paper to present the results of an investigation comparing the qualities of three of the most recent and promising of these drugs.

It is not difficult for the chemist to develop new and highly active local anesthetics; however, it is difficult to develop a drug which is not unusually toxic or which does not have tissue irritating properties. Many hundreds of active anesthetic compounds have been synthesized since procaine (1), but only a few have been acceptable for clinical use. Perhaps workers have concentrated on improving the known compounds rather than pursuing a different and original course of investigation. This may be concluded on the basis that the majority of accepted and effective local anesthetic drugs are of similar chemical nature, being either esters or amides of aromatic carbonic acids. Procaine is still the most widely used local anesthetic agent; it is classified as a rather inactive drug and listed among the weaker local anesthetic agents. The wide success attained with its use is based on an unusually low toxicity and a lack of tissue irritation.

The concentrations of the solutions furnished by the respective manufacturers of these drugs are within what they believe a safe and

* Xylocaine is the trade name of the Astra Pharmaceutical Company. The nonproprietary name is lidocaine.

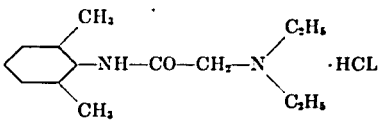
† Cyclaine is the trade name of Sharp and Dohme. Hexlycaine is the nonproprietary name.

‡ Pravocaine is the trade mark of Winthrop-Stearns, Inc. and furnished to the investigators as WIN 3459-2. See addendum

effective range, based on laboratory experiments. Unfortunately, the results obtained in the laboratory on experimental animals do not always directly apply to human beings. This was true in some portions of this investigation, as will be seen in subsequent paragraphs.

XYLOCAINE®

Xylocaine® was synthetized by Löefgren (2) in 1943 and listed as LL30. It is a derivation of acetanilide and differs in structure from the cocaine and procaine group. The chemical structure is:



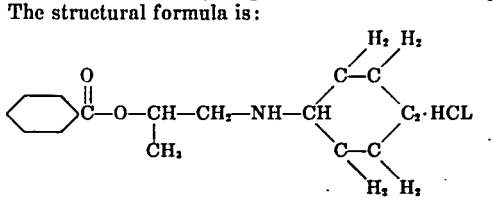
ω-diethylamino-2,6-dimethylacetanilide hydrochloride

It is supplied in solutions varying from 0.5 per cent to 2 per cent for conduction anesthesia. The solutions may be obtained with or without epinephrine and are extremely stable. Ampules for spinal anesthesia are available in Sweden, but are not at present manufactured in the United States. Solutions of 3 per cent to 5 per cent concentrations are available on request. The pH is 7.0 without epinephrine and 3.5 to 4 with epinephrine. The specific gravity varies from 1.0057 in a 1 per cent solution without epinephrine to 1.0077 in the 2 per cent solution with epinephrine.

The properties of xylocaine according to laboratory data (3) are: (1) it is the most stable anesthetic agent known and may be stored almost indefinitely or vigorously heated in the presence of strong alkalis or acids; (2) it has an unusually short latency period; (3) it has wide clinical usefulness and is adaptable to all types of conduction anesthesia; (4) it has rapid diffusion qualities; (5) it is of relatively low toxicity, and (6) it produces profound anesthesia.

CYCLAINE®

Cyclaine® was synthetized by Cope and Hancock and reported in 1944 (4). The structural formula is:



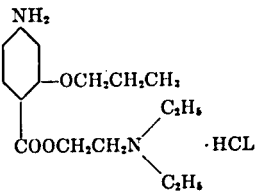
1-cyclohexylamino-2-propylbenzoate hydrochloride

According to the laboratory data (5), it is soluble as a hydrochloride to the extent of about 12 per cent. A one per cent solution of the hydrochloride is stable to boiling and autoclaving for sterilization. It is reported to have the following advantages: (1) a toxicity comparable to procaine and metycaine; (2) topical activity comparable to cocaine and butacaine; (3) a duration of anesthesia second only to tetracaine, and (4) stability during sterilization of solutions.

Cyclaine is supplied in vials of 50 cc. of a 1 per cent solution for infiltration and 5 cc. vials of 5 per cent solution for topical anesthesia. These vials do not contain epinephrine. A 5 cc. ampule of 1 per cent cyclaine and 10 per cent dextrose is available for spinal anesthesia. The pH of one per cent cyclaine is 3.9 and the pH of 5 per cent cyclaine is 3.7.

PRAVOCAINE®

The addition of a two propoxy group to procaine results in this compound, pravocaine®, whose structural formula is:



2-diethylaminoethyl-4-amino-2-propoxybenzoate hydrochloride

Pravocaine is a white, crystalline solid which melts at 148.3 to 150.0 C. (corrected). It is soluble in water to the extent of at least 20 per cent. The pH of a 1.0 per cent solution is 5.5 and when adjusted with 0.1 normal sodium hydroxide, it does not precipitate. According to laboratory data (6), it possesses: (1) an activity halfway between that of procaine and cocaine; (2) a topical activity one and one-half times that of cocaine; (3) the same toxicity as tetracaine, and (4) about one-fourth the irritating actions of tetracaine.

Pravocaine is supplied in 30 cc. vials of 0.1 and 0.2 per cent solutions with epinephrine hydrochloride 1:200,000, as well as in 5 cc. ampules containing 3 mg. per cubic centimeter in 10 per cent dextrose.

CLINICAL APPLICATION

The three drugs have been used in varied technics for a total of 1,233 administrations (table 1). Peridural anesthesia furnished the largest series and offered the most valuable method for comparing their clinical effectiveness.

TABLE 1

Infiltration	186
Brachial plexus block	34
Peridural blocks (for abdominal, thoracic and perineal surgery)	661
Topical	
Cystoscopy and bronchoscopy	288
Reginal nerve blocks	37
Spinal anesthesia	27
Total	1,233

Skin wheals constituted the first comparative study to which these drugs were subjected. A volume of 0.3 cc. without epinephrine was used for each wheal, and the reported duration was obtained from 10 administrations of the designated drug and concentration (table 2), the purpose being to correlate the duration of action of the various drugs in respect to different concentrations. The duration with cyclaine was more than twice that of xylocaine and procaine in similar concentrations. Pravocaine gave the longest duration of action in low concentrations, but was available only in 0.1 and 0.2 per cent solutions and, therefore, an extensive comparison was not possible. It may be noted that the duration of action of xylocaine was slightly greater than that of procaine in the skin wheals. No local or systemic reactions were noted. The addition of epinephrine, 1:100,000, prolonged the duration of analgesia of each drug three to six times.

Latency Period.—The interval of time elapsing between the administration of an anesthetic and the onset of anesthesia is a major problem to the physicians involved in the busy operating schedule. Any drug that shortens this interval to any practical degree offers a definite contribution to the future of regional anesthesia. Two such drugs are xylocaine and cyclaine. The interval with xylocaine is about five to eight minutes, using 2 per cent solutions, and increases to about eight to ten minutes with the more dilute solutions. The addition of epinephrine delays the onset slightly. The latency period of cyclaine on some occasions equals that of xylocaine, but is not con-

TABLE 2

DURATION IN MINUTES OF SKIN WHEALS

Concentration of Solution, per cent	Cyclaine	Pravocaine	Xylocaine	Procaine
2.0	146	Not available	47	43
1.0	76	Not available	33	31
0.5	52	Not available	27	24
0.25	43	Not available	21	19
0.2	39	50	18	Not profound
0.1	19	33	13	Not profound

sistent—from seven to thirteen minutes. Pravocaine has an average latency period of thirteen to fifteen minutes. The unusual characteristic of this drug is its variable effect; it is not unusual to obtain complete and excellent epidural blocks with motor involvement in seven to eight minutes in one patient, while in the next patient twenty minutes may be required to produce sensory analgesia.

Stability.—Xylocaine is stable for storage over a period of years and may be sterilized by autoclaving or boiling without deteriorating. The solutions containing epinephrine have been prepared in a special manner by Karlsson and Sjogren (7) and are therefore stable. Cyclaine is unstable for storage. In a period of less than four months, solutions will deteriorate and appear to change from clear to pink. A 1 per cent solution will tolerate a moderate sterilization procedure.§ The stability of pravocaine is believed to be more stable that its parent compound, procaine, but definite evidence of its over-all stability is not available. There has been no evidence of deterioration in the ampules which were shelved over eight months.

TABLE 3

COMPARATIVE QUALITIES

Local Anesthetic Agents	Latency Period	Stability	Topical Effect	Duration	Profoundness of Anesthesia	Toxicity	Activity
Xylocaine®	1	1	1	2	1	2	3
Cyclaine®	2	4	2	1	2	3	2
Pravocaine®	3	2	3	3	3–4	4	1
Procaine	4	3	4	4	3–4	1	4

Topical Effect.—Comparing the qualities of similar compounds presented innumerable problems. It is not difficult to classify drugs which have varied clinical results when submitted to identical studies, but when two or more drugs react in a similar manner, it is almost impossible to give one a preferential listing. This is particularly true when conclusions are based primarily on subjective rather than objective data, as is necessary in measuring topical activity. In such instance as the latter, care was exercised in selecting patients who had had previous experience with another drug to serve as basis for their classification. The subjective statements were weighed in regard to their source considering the stability of the patient.

Bronchoscopy and cystoscopy were selected for comparing topical activities. The physicians performing these procedures were particularly pleased with the short latency period associated with cyclaine and xylocaine and were even more pleased with the analgesia. The opinions of two urologists and four bronchoscopists concerning the

§ Loss of potency does not exceed 2 per cent after 6 months storage or two standard autoclavings. The pink discoloration is now believed to be insignificant.

comparative topical activities are listed in table 3. The two urologists were more impressed with cyclaine, but believed there was little difference between the agents. The bronchoscopists favored xylocaine. It should be noticed that xylocaine was used in 2 per cent solutions and cyclaine was a 5 per cent solution. When cyclaine was used as a 2 per cent solution there was a very noticeable difference and xylocaine was listed a superior anesthetic by the urologists and bronchoscopists. No untoward reactions have been encountered. Since the toxicity of xylocaine is less than that of cyclaine and the use of a 2 per cent solution of xylocaine is superior to a 2 per cent solution of cyclaine, it must be concluded that xylocaine is superior in its topical effect. The main disadvantage of xylocaine is its short duration of action when used in this manner (fifteen to twenty minutes). The duration of the topical action of cyclaine is considerably greater. We were unable to produce a satisfactory topical anesthetic with either a 0.1 per cent or 0.2 per cent solution of pravocaine.

Duration.—The duration of anesthesia is greatest with cyclaine, which resembles pontocaine in this respect. The prolongation of anesthesia keeps pace with the increase in concentrations of the drug to a far greater extent than with xylocaine or pravocaine. At low concentrations, cyclaine offers approximately the same duration of anesthesia as xylocaine. However, as the concentrations increase, the duration of anesthesia with cyclaine is increasingly greater than with xylocaine. Anesthesia produced by pravocaine is of longer duration than that by xylocaine and close to cyclaine in equal concentrations; however, the toxicity of pravocaine necessitates its use in dilute solutions of approximately one-eighth the other two drugs and, therefore, its actual duration is less.

The addition of epinephrine in 1:100,000 concentration prolongs the duration of anesthesia produced by all three drugs approximately 30 to 50 per cent.

Profoundness of Anesthesia.—The profoundness of anesthesia is primarily a subjective finding that is extremely hard to evaluate. It is usually accepted as being proportionate to the concentration of the solution. Sensory anesthesia begins with the weaker concentrations and progresses to complete motor paralysis as the concentration increases. The anesthesia resulting from xylocaine consistently impressed the anesthesiologist with its seemingly profound nature. Any dosages that were strong enough to offer good sensory block gave this impression. This has not been true of any other local anesthetic drug. Through the use of a catheter within the peridural space, it has been possible to verify these clinical impressions.

Case 1.—A 37 year old woman who was to have a pulmonary resection of the left lower lobe was given an injection of 30 cc. of a 0.5 per cent cyclaine solution without epinephrine. It is noted that with the varied concentrations, epinephrine may or may not be added. This is done to compare the effective-

ness and duration of different combinations of drugs. The patient complained of discomfort in the operative site, but the pain was vague and she was unable to describe it. After fifty-six minutes of operating she complained of a burning sensation in the skin area supplied by the fifth intercostal nerve anteriorly, and 30 cc. of 0.5 per cent xylocaine with epinephrine was administered through the catheter. In five minutes she was free from pain when questioned, volunteered the following statement: "I am not having any pain since they quit operating." The surgeon was in the midst of the operative procedure. The patient remained pain free throughout the operation. Subsequent injections of 30 cc. of 0.5 per cent xylocaine with epinephrine were given at one hour intervals.

Case 2.—A large, 41 year old man was given a peridural anesthetic consisting of 30 cc. of 0.6 per cent cyclaine without epinephrine for a first stage thoracoplasty. The patient complained of discomfort when the incision was made and it was decided that the volume of solution might have been inadequate. Within twenty-seven minutes of the original injection, another 10 cc. of 0.6 per cent cyclaine was given. No further relief was obtained with this injection. Following removal of the second and third ribs and before removal of the first rib (fifty-two minutes after the original injection), a 30 cc. volume of 0.6 per cent xylocaine with epinephrine was given. Within five minutes, the patient was free of pain and stated that he could not feel the surgeons operating. The first rib was being removed at that time.

Case 3.—A 70 year old woman was given 30 cc. of 1 per cent cyclaine without epinephrine through a plastic tubing placed within the epidural space at the sixth thoracic segment for exploration of the gallbladder and common bile duct. The patient was restless and expressed discomfort at the time of the incision and exploration. Relaxation was inadequate. Thirty minutes after the original injection, 30 cc. of 1 per cent xylocaine without epinephrine was administered through the plastic tubing. Within seven minutes, the patient relaxed and remained free from pain throughout the surgical procedure.

Cyclaine in concentrations of 0.8 to 1 per cent usually offered a complete and satisfactory peridural anesthesia in the thoracic area. However, in a number of instances, attempts were made to confuse the patient by alternating injections of xylocaine and of cyclaine of similar concentrations. The patient often distinguished between the two agents. In view of the short latency periods and high activity of the agents, it was difficult to explain this difference except by the excellent diffusion qualities characteristic of xylocaine. Although it is possible that a systemic reaction to the drug was taking place, there was no evidence to support this for these patients were oriented and awake (see Comment).

Toxicity.—The toxicity studies listed in table 2 were not derived from clinical experience, but based on laboratory data, as designated. Xylocaine has a toxicity equal to procaine in concentrations of 0.5 per cent or less. As the concentration increases, its toxicity exceeds that of procaine. At 1 per cent it is 40 per cent greater, and at 2 per cent it is 50 per cent greater (8). Studies on acute intravenous toxicity (6) show xylocaine to be approximately twice as toxic as procaine. Xylocaine is considerably more active and effective than procaine and, therefore, may be used in smaller dosages. Its relative toxicity,

therefore, is less than procaine and offers a safety coefficient (9) two to four times higher.

According to the intravenous toxicity studies of Beyer (5) cyclaine is placed between procaine and cocaine and is three times as toxic as procaine. However, in subcutaneous administration, the proportion is not nearly as great and its toxicity more closely resembles that of procaine. Cyclaine possesses greater activity and may be used in more dilute solutions, resulting in a lower relative toxicity.

According to the laboratory data (6), the toxicity of pravocaine and of pontocaine given intravenously is the same. Tetracaine and pravocaine are about ten times more toxic than procaine. This accounts for the use of this drug in 0.1 and 0.2 per cent solutions to stay in a range of relative toxicity equal to that of procaine.

TABLE 4

RESULTS OF THE USE OF XYLOCAINE IN PERIDURAL ANESTHESIA

Concentration of Drug, per cent	Average Duration, minutes		Resulting Anesthesia in		
	With Epinephrine	Without Epinephrine	Thoracic Surgery	Abdominal Surgery	Perineal Surgery
2.0	155	85	Unable to use Concentration too high	Excellent	Excellent
1.5	120	70	Too concentrated	Good to excellent	Excellent
1.25	115	65	Too concentrated	Good	Excellent
1.0	90	60	Usable, but concentration too high	Fair	Excellent
0.8	70	50	Excellent	Inadequate	Excellent
0.7	60	45	Good to excellent	Inadequate	Excellent
0.6	55	40	Good	Inadequate	Excellent
0.5	50	35	Fair to *good*	Inadequate	Good
0.4	Unable to measure	Unable to measure	Inadequate	Inadequate	Poor to fair
0.25	Unable to measure	Unable to measure	Inadequate	Inadequate	Inadequate

Previous experience using large doses (30 cc. containing 500 to 600 mg.) of procaine for peridural anesthesia occasionally resulted in mild reactions. These reactions have almost been eliminated since using xylocaine and cyclaine (240 to 300 mg.). This is attributed to the lower relative toxicity of the latter drug.

Activity.—The minimal effective concentration of a drug is the index most commonly used for judging activity. The dose response curve, then, can be utilized to obtain comparative qualities. Pravocaine has the lowest effective concentrations, with cyclaine, xylocaine and procaine following in that order.

Regional Anesthesia.—The most practical method for comparing the ability of these drugs to interrupt nerve conduction would be a technic in which the anesthetic drug would be deposited in an area

where nerve tissues would definitely be exposed. The vertebral canal appeared to be the obvious place, and a choice was necessary between subarachnoid and peridural anesthesia. Subarachnoid block is usually rapid in onset and profound, thereby offering difficulty in comparing the effectiveness of various drugs. Peridural anesthesia has always presented annoying problems to the surgeon and anesthesiologist, foremost of which are: (1) the increased technical difficulty in performing a successful block, (2) the relatively high incidence of complete failures and partial blocks and (3) the prolonged latency period. The peridural space serves only as a reservoir for the anesthetic drug which must extend to the paravertebral space before conduction is blocked, thus offering an opportunity to compare features of drugs that would be difficult to check in a subarachnoid block. Each drug was tested in varied concentrations in an effort to determine optimal concentrations for dif-

TABLE 5

RESULTS OF THE USE OF CYCLAINE IN PERIDURAL ANESTHESIA

Concentration of Drug, per cent	Average Duration, minutes		Resulting Anesthesia in		
	With Epinephrine	Without Epinephrine	Thoracic Surgery	Abdominal Surgery	Perineal Surgery
1.5	145	95	Unable to use	Good to excellent	Excellent
1.0	105	80	Excellent	Fair to good	Excellent
0.8	90	70	Good	Fair	Excellent
0.7	75	60	Fair to good	Inadequate	Excellent
0.6	60	50	Fair	Inadequate	Good
0.5	50	40	Poor to Fair	Inadequate	Good
0.4	Unable to measure	Unable to measure	Inadequate	Inadequate	Inadequate
0.25	Unable to measure	Unable to measure	Inadequate	Inadequate	Inadequate

ferent operative sites. The average duration of anesthesia which can be expected from each concentration with and without epinephrine is listed. The resulting anesthesia was evaluated by descriptive words in an effort to demonstrate the proper concentrations of drug necessary to produce an optimal block at that surgical site. In thoracic blocks, sensory anesthesia must be provided without causing motor involvement. Therefore, heavy concentrations cannot be used (10). In abdominal surgery, relaxation is needed and, therefore, greater concentrations are used. In perineal surgery, varied demands are made. If relaxation is needed, a more concentrated solution is used than for sensory anesthesia.

It may be seen in table 4 that xylocaine in solutions of from 0.5 to 1.0 per cent is excellent for thoracic surgery, but if abdominal exploration is to be performed a 1.25 to 2 per cent solution is needed in order that the motor nerves be blocked. These statistics were gathered

TABLE 6

RESULTS OF THE USE OF PRAVOCAINE IN PERIDURAL ANESTHESIA

Concentration of Drug, per cent	Average Duration, minutes		Resulting Anesthesia in		
	With Epinephrine	Without Epinephrine	Thoracic Surgery	Abdominal Surgery	Perineal Surgery
0.2	70	50	Fair to good	Inadequate	Good
0.1	55	40	Inadequate	Inadequate	Fair

through the use of an indwelling plastic catheter which permitted serial injections. In table 5 the concentrations of cyclaine are compared in a manner similar to that shown in table 4. The longer duration of anesthesia with cyclaine is demonstrated and the resulting anesthesia may be compared. Table 6 gives the same comparison for pravocaine. From these three tables, it is possible to choose the optimal concentration of each drug for a given field and to predict the duration of anesthesia which will result.

My experience with these drugs for spinal anesthesia is not of sufficient magnitude to be reported at this time. Dosages are listed in table 7.

In brachial plexus block, xylocaine acted faster and anesthesia was more profound than the other drugs. It was used in 1 per cent solutions for children and the aged, and when sensory rather than complete motor block was requested. A 1.5 to 2 per cent solution was used in average adults. The duration of anesthesia varied from two hours when 1 per cent solution without epinephrine was used to three and one-half hours when a 2 per cent solution containing epinephrine was employed. The total volume should be less than 50 cc. of 1 per cent or 25 cc. of 2 per cent solution. The addition of epinephrine to large volumes was found to be desirable and should be used if no

TABLE 7

EFFECTIVE CONCENTRATIONS

Technic	Xylocaine	Cyclaine	Pravocaine[1]
Infiltration	0.25%	0.25 to 0.5%	0.1%
Epidural block for thoracic surgery	0.8%	0.8 to 1.0	0.2%
Epidural block for abdominal surgery	1.25 to 2%	1.5%	0.2%
Epidural block for perineal surgery	1%	1%	0.2%
Brachial plexus block	1.0 to 1.5%	1%	0.2%
Topical use	2 to 5%	2 to 5%	?
Spinal anesthesia	10-20 mg. per cc. with dextrose	25 mg. per cc. with dextrose	3 mg. per cc. with dextrose

[1] See addendum.

contraindications to its use are present. Cyclaine administered in the same manner as xylocaine produced anesthesia approximately 50 per cent longer in duration and the onset was almost as rapid. Pravocaine had no advantages to offer and resembled procaine in its actions.

Infiltration.—An unusual amount of discretion and care must be exercised in the selection of a concentration of local anesthetic drugs for infiltration purposes. For fifty years, procaine has been used as the drug of choice, and because of its low activity and toxicity, large volumes of dilute solutions have been used with relatively few untoward reactions. It is not unusual to employ 100 to 200 cc. of 0.5 per cent procaine for infiltration anesthesia in a major procedure in which it is used as the primary anesthetic agent. The technics now employed by most physicians are adapted to the use of procaine and when other drugs of higher toxicity are substituted, using similar concentrations and volumes, a greater incidence of reactions must be expected. Epinephrine should be used with large volumes of solutions in vascular areas to delay absorption and prolong the duration of anesthesia.

Cyclaine in 1 per cent solution has been proposed for infiltration. This is unnecessarily high, and when surgeons and anesthetists substitute the drug for procaine with no regard to the toxicity, reactions will occur. This is also true with xylocaine. It is manufactured in a 0.5 per cent solution for infiltration and the literature furnished with the drug suggests that its total dosages are comparable to those for procaine (0.5 Gm.); however, it is also stated that if over 100 cc. of solution is to be used, the concentration should be limited to 0.25 per cent. Unfortunately, the accompanying literature is not always read or followed and as a result a drug receives unfounded condemnation. Recently, a death which occurred after regional infiltration was reported in the British Medical Journal (11). In less than fifteen minutes 80 cc. of a 0.8 per cent solution of xylocaine without epinephrine was injected into a vascular area. This patient had previously had a thoracoplasty for which she had received 100 cc. of a 0.5 per cent solution of xylocaine with epinephrine, with no untoward reactions. This is an excellent example of the indiscriminate use of this drug. Recently, an anesthesiologist stated that he had found a high incidence of reactions to xylocaine in infiltration anesthesia. Questioning revealed that he often used 125 to 150 cc. of a 0.5 per cent solution of xylocaine with and without epinephrine. The same technics and volumes were employed as when a 0.5 per cent solution of procaine was used, with no regard to toxicity or diffusion qualities. Both drugs are more toxic and possess a greater activity than procaine and should be used in smaller concentrations. Xylocaine should be used in less volume as well as less concentration because of its properties of diffusion which result in a greater area being blocked, per unit, than with any other local anesthetic drug.

Pravocaine is supplied in a 0.1 per cent solution which is satisfactory for infiltration. It is obvious that this concentration is in correlation with its activity and toxicity.

Systemic Reaction.—One feature not mentioned in the previous discussion is the type of systemic reactions which occur with xylocaine. All local anesthetic agents have demonstrated similar symptoms when administered in toxic amounts. Initially, the central nervous system is stimulated, which progresses to convulsion, followed by suppression and death as a result of respiratory failure. Xylocaine seems to produce a depression rather than stimulation of the central nervous system as an initial effect. This depression can progress to the convulsive stage and eventually death in the more severe reaction. It is often noted that patients are drowsy following large doses of xylocaine; this effect is believed to be a result of the circulating drug which has been absorbed and is on its way to being detoxified. This drowsiness is believed to be a very desirable property and considerable attention is given to it by investigators.

COMMENT

Xylocaine has proved to be the outstanding local anesthetic drug among the drugs presented. It may also be concluded on reviewing its properties that it is superior to any existing local anesthetic drug.

Xylocaine should be used in lower concentrations than procaine because of its greater activity and toxicity. Xylocaine should be used in half or less than half the concentrations of procaine and, with the exception of peridural and subarachnoid blocks, it should be employed one-half to two-thirds the volumes of procaine used for similar procedures.

The outstanding features of xylocaine are: (1) rapid onset of anesthesia; (2) marked stability; (3) widespread clinical utility; (4) high activity with a comparatively low toxicity giving a low relative toxicity; (5) profoundness of anesthesia and (6) drowsiness associated with its use.

Cyclaine appears to be a close second to xylocaine. Anesthesia is comparatively rapid in onset, and cyclaine offers a long duration of action and compares in toxicity to procaine and xylocaine. Resulting anesthesia is not as profound as that produced by xylocaine, nor does it possess the diffusion action so characteristic of xylocaine. Cyclaine is far superior to any local anesthetic drug other than xylocaine and offers a duration of anesthesia which makes it most desirable. Xylocaine and cyclaine should be used in similar concentrations and total dosages.

It would be a gross injustice to make a conclusive statement either praising or condemning pravocaine. Clinically, it proved to be similar to procaine. The onset of anesthesia is slightly more rapid, its duration greater and the drug possesses a higher topical activity;

however, it is considerably more toxic than procaine. I believe that better results were not obtained with pravocaine because it was used in too dilute solutions. A further clinical trial is indicated, using concentrations of 0.5 to 1 per cent.

SUMMARY

The physical properties and chemical structure of three new anesthetic drugs have been presented.

Efforts have been made to compare these drugs numerically in regard to the various qualities desirable in a local anesthetic agent.

The use of xylocaine, cyclaine and pravocaine in peridural anesthesia has been graphically illustrated to show: (1) duration of anesthesia, with and without epinephrine, and in various concentrations and (2) the usefulness of each drug in various concentration and operative fields.

Effective concentrations for each of the three drugs in the various methods of application, based on relative toxicity and activity, are suggested.

The over-all efficiency and superiority of xylocaine are discussed and compared with cyclaine and pravocaine.

ADDENDUM

The name of the drug listed as "pravocaine" throughout this article has recently been changed to "ravocaine" and furnished in solutions of greater concentration (0.5 per cent). To date this new concentration has been used only in peridural anesthesia. The results thus far are definitely more impressive than with the lower concentrations, and no untoward reactions have been noted.

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