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# Comparison of the Systemic Effects of Local Anesthesia with and without Epinephrine in Children

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# COMPARISON OF THE SYSTEMIC EFFECTS OF LOCAL ANESTHESIA WITH AND WITHOUT EPINEPHRINE IN CHILDREN

BY

Robert A. Swanson, D.D.S.

A Thesis Submitted to the Faculty of the Graduate School of Loyola University of Chicago in Partial Fulfillment of the Requirements for the Degree of

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The author, Robert A. Swanson, is the son of Dr. Adrian L. Swanson and Margaret A. Swanson. He was born April 5, 1950, in Evanston, Illinois.

His elementary education was obtained in the public schools of Wilmette, Ill., and secondary education at New Trier Township High School, Winnetka, Ill., where he graduated in 1968. In September, 1968, he entered the University of Colorado and in May, 1973, received the degree of Bachelor of Arts in biology.

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#### INTRODUCTION

In 1924 Braun first introduced the use of the vasoconstrictor in local anesthetic solutions because procaine was found to be short acting due to rapid diffusion. He found that the addition of minute amounts epinephrine (1:100,000-1:200,000) resulted in longer lasting and more satisfactory anesthetic properties.

Since that time there has been concern over the cardiovascular effects produced by epinepherine. Several studies have been conducted to determine whether this concern is warranted. The subjects for these studies, however, have all been adults (normotensive, hypertensive, and those with cardiac disease). No studies concerning epinephrine have utilized children as subjects. It would seem that children, due to their smaller size and different metabolic rates, might be more susceptible to the effects of epinepherine when injected with the same or slightly smaller doses. It is the intent of this study to monitor blood pressure, heart rate, and galvanic skin response for changes caused by the addition of epinephrine to a local anesthetic solution and to determine which anesthetic solution is most comfortable and effective for use with children.

#### REVIEW OF RELATED LITERATURE

#### Secretion and Elimination of Epinephrine

Epinephrine is normally secreted by the resting adrenal medulla at the rate of approximately 0.2 mg/kg/min. (Guyton, 1976). It is rapidly metabolized by catechol-0-methyl-transferase and monoamineoxidase in various tissues of the body (mainly the liver) and the metabolic products are excreted through the kidneys. A dose of 0.1 mg./kg. of epinephrine given intravenously is completely metabolized within ten minutes and smaller doses in less time. The biological half-life for epinephrine is less than one minute (Glover, 1968).

Under normal resting conditions, the catecholamine concentration (primarily epinephrine) is 0.1-1.0 micrograms/liter of blood. With pain, excitement, anxiety, anoxia, or similar stresses, the concentration increases to as much as 100 micrograms/liter of blood (Selkurt, 1971). Under these conditions, all properties of the heart are stimulated, including pulse rate, automaticity, excitability, and contractility. Also apparent are increased cardiac output, a rise in blood pressure, and increased metabolism (Monheim, 1966).

#### Adrenergic Receptor Sites

In 1948 Ahlquist proposed the existence of two types of adrenergic receptors which he designated "alpha" and "beta". He proposed that the activation of alpha receptors by an adrenergic drug caused one type of response and the activation of beta receptors caused a

different response. The action of alpha receptors is generally excitatory on smooth muscle. The exception to this statement is that alpha receptors in the gastrointestinal tract produce intestinal relaxation when stimulated. Excitation of beta receptors is usually inhibitory to smooth muscle and excitatory to cardiac muscle.

Most tissues have both alpha and beta receptors. The response of a certain tissue depends primarily on the majority of the receptor types present. For example, smooth muscle of blood vessels in the skin and mucosa exhibits primarily alpha receptors and, thus, responds to epinephrine with vasoconstriction. Smooth muscle of blood vessels in skeletal muscle has a majority of beta receptors and responds to epinephrine with vasodilation. The receptors in the heart are of the beta type and respond with increased heart rate and strength of contraction (Holroyd, 1974).

Goodman and Gilman (1975) state that 1.5-1.0 mg. of epinephrine, injected subcutaneously (or .Ol-.03 micrograms, intravenous infusion), may cause cardiac output to increase but, due to dilation in some blood vessels (a decrease in peripheral vascular resistance), blood pressure is usually not greatly elevated. This is primarily due "to the greater sensitivity to epinephrine of beta receptors in vascular beds dilated by the drug than of alpha receptors in vascular beds constricted by it" (Goodman and Gilman, 1970). Their fifth edition (1975) states that "diastolic blood pressure usually falls" with subcutaneous doses as large as 0.5-1.5 mg.

Ordinarily the vasodilator effect of epinephrine dominates the circulation, and the rise in systolic pressure is largely due to an increased cardiac output. With increasing dosages there may be no change or even a rise in peripheral resistance and diastolic pressure which is attributed to the increased participation of alpha receptors when compared to beta receptors in various vascular beds.

#### Epinephrine in Local Anesthesia

There are two schools of thought concerning the use of epinephrine in local anesthesia. The first is concerned with the physiological changes produced by exogenous epinephrine, particularily in hypertensive patients and patients with cardiovascular disease.

In an early investigation, Miller et al., (1938) subjected 26 patients (13 subjects and 13 controls), aged 16-70, to mandibular blocks and reported minor changes in heart rhythm and in the T waves of the electrocardiogram when using 2-9 cc. of 2% procaine with 1:50,000 (.04-.18 mg.) epinephrine. A higher concentration of epinephrine, 1:20,000 (.08-.4 mg.), produced greater T wave changes while Ringer's solution produced no changes.

When a solution containing epinephrine is intravenously infused tnto a normal adult at such a rate that the patient receives about .01-.02 mg./min. for three minutes, the following hemodynamic changes will generally be observed: systolic pressure increases, diastolic pressure decreases, mean pressure remains unchanged, and cardiac output increases approximately 5-6 minutes after infusion (Barcroft, 1949).

White (1952) states that 0.5 mg. of epinephrine is the effective dose for pressor effects in normal adults when injected subcutaneously.

McCarthy (1957) studied cardiovascular changes in 40 male subjects, aged 21-32, using 5cc. of 2% procaine with and without 1:50,000 epinephrine (.1 mg), 2% lidocaine with and without 1:100,000 epinephrine (.05 mg), an isotonic saline solution, and a pseudoinjection for a control. These solutions were deposited at buccal and palatine injection sites. He reported no pressor responses but noted a significant fall in diastolic pressure during the 10 minutes after injection which he attributed to the depressing effect of small amounts of exogenous epinephrine causing a decrease in peripheral resistance.

Kennedy (1966) demonstrated major cardiovascular changes on 30 adult patients (15 subjects and 15 controls) with doses of epinephrine ranging from ,025 to .4 mg. in the brachial plexus and epidural blocks. These changes included significant decreases in mean arterial pressure, increases in heart rate, increases in cardiac output, and decreases in peripheral resistance.

Using 2% Lignocaine (lidocaine) with 1:80,000 epinephrine (mean injected volume of 5.9 ml. (about .08 mg.) on adult subjects undergoing oral surgery, Aellig (1970) found an increase of between 5 and 40 beats/ min. in the pulse rate of all 27 subjects. In a similar experiment, Persson (1969} reported that 10% of his subjects experienced electrocardiographic changes and/or other side effects.

Allen et al., (1973) used 1.8 ml. of 2% lidocaine with and without 1:100,000 (.018 mg.) epinephrine for inferior alveolar nerve blocks on subjects between 21 and 38 years of age. He found no changes in the mean arterial pressure or pulse rate but, using Jorgenson and Shane techniques, did find a rise in stroke volume 5 and 15 minutes after injection and a fall in diastolic blood pressure due to decreased peripheral resistance. Allen did not substantiate conclusions that fear and anxiety produced greater changes in cardiorespiratory effects than exogenous epinephrine.

The second school of thought believes that the amounts of epinephrine used in local dental anesthesia are too small to be of physiological importance. Furthermore, these small amounts of epinephrine provide a longer period of anesthesia. Dental anesthesia produced with 2% lignocaine hydrochloride lasts about 20 minutes, but the addition of 1:80,000 (about .015 mg.) epinephrine prolongs the effects to an hour and a half or more (British Medical Journal, 1970 and Gangarosa, 1967}.

Bjorn and Hullet (1947) found an increased efficiency of anesthesia with increased epinephrine (1:40,000 or .02 mg./cc.) for 1% lidocaine. Gangarosa (1967), however, reported no clinical advantage between 1:100,000 (.01 mg./cc.) and 1:300,000 (.004 mg./cc.) epinephrine in lidocaine solutions.

Wallace et al., (1956) investigated the difference in the cardiovascular system resulting from the use of 2.1 cc of 2% procaine with

and without 1:50,000 (.02 mg./cc.} epinephrine. Using 19 healthy students, Wallace and coworkers took automatic continuous recordings of finger plethysmography, pneumography, unipolar frontal and occipital electro encephalograms, and standard electrocardiogram determinations. Systolic and diastolic pressures were measured with a cuff at two minute intervals. Their conclusions were that there were no clinically significant systemic cardiovascular changes.

Cheraskin (1958} reported, under simulated office procedures, that there was little variation in systolic, diastolic, mean, and pulse pressures and in pulse rate at 5 and 10 minute intervals after injection of 2 to 8 cc. of 2% lidocaine with and without 1:100,000 (.02-.08 mg.) epinephrine in 136 normotensive and hypertensive patients. In a study on 142 sedated hypertensive patients, Cheraskin (1959} found that 2% lidocaine with epinephrine produced less cardiovascular effects than lidocaine without epinephrine.

Elliot and Stein (1974), using 40 patients aged 39-78 with histories of atherosclerotic heart disease, found no significant differences in blood pressure, heart rate, and electrocardiograms 1, 5, and 10 minutes after injection of 1.8 cc of 2% lidocaine hydrochloride with and without 1:50,000 (.04 mg.) epinephrine.

The New York Heart Association states that 0.2 mg. of epinephrine is the maximum total dosage for cardiac patients (Holroyd, 1960). The opinion expressed in Accepted Dental Therapeutics (1977) is that concern over the small amounts of epinephrine in local anesthetic

solutions used for dentistry is unwarranted.

Holroyd (1960) states that the cardiovascular effects of epinephrine in local anesthesia have been subject to many investigations which concluded that inadequate local anesthesia would cause the production of more endogenous epinephrine than the quantity injected. Emotional stresses such as pain, fear, and anxiety produce a natural secretion of epinephrine into the blood and this quantity is much greater than that found in the average dental anesthetic (Orringer, 1949; Dick, 1953). Several investigators state that local anesthetic solutions without a vasoconstrictor are not satisfactory because the likelihood of pain is much greater due to their uncertain or incomplete anesthesia (Tainter, 1940; Orringer, 1949; Dick, 1953; and Brown, 1968).

The British Medical Journal (1970) concludes that so long as local anesthetics containing vasoconstrictors are never used in the finger, toe, ear, or other areas of restricted circulation and are injected subcutaneously in doses not exceeding .5 mg. they are largely free of risk and the more prolonged anesthesia produced greatly extends their usefulness. It also indicates that .025 mg. of epinephrine in a dental nerve block would be absorbed slowly over a 2 hour period into the circulation and no effects should be expected.

In summary, although there is argument over the use of epinephrine in local dental anesthetic solutions, it appears that the disagreement is fundamentally based on the dosage and route of injection. Those studies that demonstrated systemic cardiovascular changes were

were based on using subcutaneous routes with dosages ranging from .025 to .4 mg. or on using intravenous routes with dosages as small as .01 - .02 mg. The other studies which did not demonstrate cardiovascular changes used subcutaneous routes with dosages from .004 mg. to .08 mg.

### Galvanic Skin Response

The galvanic skin response (GSR) is an indicator of emotional tension which has been used primarily in conjunction with the lie detector. The measurement of the GSR is made by passing a small electrical impulse across the skin between two electrodes. The electrical resistance of the skin to the impulse decreases as sweating increases and this, in turn, produces a deflection in the recording (Lewis and Law, 1958).

Darrow (1970) believed that the GSR involves a number of events. Following excitation, sympathetic impulses to sweat glands and the subsequent release of acetycholine account for the initial negative resistance changes while the resistance is high (before sweating has reached a critical level). These impulses, however, initiate the cholinergic response of the sweat glands and, once started, sweating is the major factor contributing to the positive potential and large decreases in skin resistance. Since sweat glands receive cholinergic sympathetic innervation, they are not expected to be stimulated by catecholamine (i.e. epinephrine)(Guyton, 1976; Goth, 1974}. According to Carmichael (1941), a decrease in skin resistance of 2500 ohms indicates

anxiety in subjects accustomed to a given testing procedure.

Jones (1948) and Lacey (1952) have both demonstrated that it is possible to measure emotional changes in children by using electronic equipment to record the GSR. In his experiment, Lacey correlated GSR to heart rate and blood pressure responses to a given stress anc concluded that the amount of response for each parameter varied for each child but was fairly consistent for a given child.

Howitt and Striker (1965) studied the physiologic changes of children aged four to seven years during simulated dental appointments. They used a modified Stoeling polygraph to record the cardiac rate and peripheral blood flow. In their report, only the cardiac rate was considered. They did not report on the results of the GSR.

#### METHODS AND MATERIALS

#### Selection of Patients

The twelve subjects for this study were chosen from the Loyola Dental School Pedodontic Department with a random distribution of race and sex. The requirements for the children were that they l) had some previous experience in the dental situation, 2) were between four and ten years of age, 3} were not excessively hyperactive, and 4) required at least two visits to the clinic for similar procedures in the maxillary arch. The parent or guardian of each child was asked to sign a standard consent form which explained the study and allowed them to withdraw their children at any time.

The procedures for this study were limited to Class I or Class II amalgam restorations or stainless steel crowns on deciduous or permanent maxillary molars. The maxillary arch was chosen over the mandibular arch because it was felt that anesthesia would be more uniform with regard to duration and quality if the anesthetic solutions were infiltrated as opposed to mandibular blocking (Grandel, 1975). No effort was made to distinguish between permanent and decicuous molars because the structure of the molar should have no effect on the nerves being anesthetized.

#### Personnel

The personnel for this study consisted of ten dental students and one investigator who was responsible for attaching the electrodes and pressor cuff to the child and operating the recording instrument.

The investigator remained in the cubicle throughout the procedure to make any necessary adjustments. Pedodontic instructors occasionally checked the dental student's progress as ts normally done in this clinic but remained no longer than was necessary.

#### Anesthetic Solutions

Anesthetic solutions in the form of 1.8 cc. carpules containing 2% xylocaine hydrochloride with or without 1:100,000 epinephrine were furnished by Astra Pharmaceutical Products, Inc.

#### Recording Eguipment

Physiologic recording equipment utilized in this study was manufactured by E. and M. Instrument Company in Houston, Texas. Physicgraph Four-A, a four channel polygraph, was used throughout the study with all four channels in operation.

The electrosphygmograph, part no. 93-400071, recorded on channel one, the photoelectric pulse pickup, part no. 91-500-700, recorded on channel two, and the galvanic skin response preamplifier, part no. 93-700-70, recorded on channel three. Channel four was used as a time and event marker. A children's size blood pressure cuff was used in conjunction with the electrosphygmograph and lead plate electrodes served as leads for the galvanic skin response.

## Experimental Method and Recording Procedure

The child was ushered into the clinic by the dental student and was seated in the dental chair in the cubicle. The investigator immediately attached the leads from the polygraph to the child, giving a simplistic explanation for each one and assuring the child that they would cause no pain. The child was then asked not to move his hands or fingers because that would shake the wires and interfere with the recordings.

The child then sat quietly for 5 to 10 minutes, neither encouraged nor discouraged from talking, while baseline recording levels were being established. Once the baselines were stable, the dental student was asked by the investigator to inject the anesthetic solution and to continue with the procedure, working at his/her own pace. Data was recorded continuously until the student was finished.

Although the patient was "in a blind" as to the anesthetic solution, the dental student was not. The choice of solution was the investigator's responsibility. The child was given one half carpule (0.9 cc.) of xylocaine either with epinephrine (1:100,000) or without epinephrine on the first visit and which ever solution remained on the second visit. The dosage of epinephrine was .01 mg., injected subcutaneously into the mucobuccal fold.

The physiologic parameters recorded in this study were heart rate, blood pressure, and galvanic skin response. Heart rate and galvanic skin response were recorded continuously throughout the procedure and blood pressure was taken at approximately five minute intervals.

Heart rate was recorded with a photoelectric pulse pickup. This device is a plethysmographic transducer which detects and records the cardiovascular pulse pressure wave. It requires direct attachment to any vascular area; in this study, the left middle finger. The

transducer connects directly to the polygraph and requires no preamplification. The pulse sensing element consists of a photoconductor and a light source mounted side by side. The light source transilluminates the area to which it is applied and the photoconductor detects changes in light intensity within the tissues caused by pulsatile variations in blood volume. This change in the light intensity reaching the photoconductor causes a change in the electrical output which is amplified and transformed into mechanical energy to deflect the pen on the polygraph.

Blood pressure was recorded by an electrosphygmograph which is a transducer/preamplifier for the recording of indirect systolic and diastolic blood pressures. It combines a pressure transducer and a preamplifier to produce single channel recordings of occluding cuff pressure and superimposed Korotkoff sounds. The electrosphygmograph was used in conjunction with a child-sized, wrap-around pressure cuff which was connected to an automatic cuff pump for blood pressure sampling. Placement for the cuff was on the child's right arm.

The galvanic skin response device is a transducer/preamplifier for recording the variations in skin resistance resulting from the reaction of the autonomic nervous system to internal and external stimuli. The skin response is obtained by measuring the resistance between two electrodes applied to the left index finger of the subject. A constant D.C. current of 20 microamperes is passed through the electrodes, and the voltage across the electrodes is then amplified and

recorded on the polygraph. With the current held constant, the voltage across the electrodes is directly proportional to the resistance between the electrodes. This device can measure skin resistance up to 1 ,000,000 ohms.

The output of the galvanic skin response preamplifier recording equipment was recorded as a direct-coupled signal. In this way, the skin resistance of the subject was balanced out and read directly on the calibrated dial. The sensitivity for the preamplifier was set at 10,000 ohms per centimeter of recording pen deflection.

#### EXPERIMENTAL RESULTS

#### Heart Rate

Heart rate was recorded for all experiments on the twelve subjects. Statistical analyses were made for the following time periods; before injection (control), at injection, 5, 10, 15, 20, 30, and 45 minutes after injection. Paired t-tests were utilized to determine

- 1) statistical differences between each time period compared to the control (baseline level before injection) for each anesthetic solution and
- 2) statistical differences between each solution at each time period.

Mean, standard deviation, mean difference (time period mean minus control mean), and p-values are presented in Tables I, II, and III.

Statistically significant decreases in heart rate are noted at 20, 30, and 45 minutes after injection without epinephrine (p<.Ol, p<.004, and p<.03, respectively).

Statistically significant decreases in heart rate are noted at 30  $(p<.05)$  and 45  $(p<.06)$  minutes after injection with epinephrine.

No statistically significant differences are noted between the two drugs at any given time period.

#### Blood Pressure

Systolic and diastolic blood pressures were recorded for all experiments on the twelve subjects. Data was analyzed for the

# HEART RATE

## 2% Xylocaine without epinephrine



\* Significant Values

# TABLE II

# HEART RATE

## 2% Xylocaine with epinephrine



# \* Significant Values

# TABLE III

# HEART RATE

Comparison of 2% Xylocaine with or without epinephrine at different time intervals



following time periods; before injection (control), 5, 10, 15, 20, 30, and 45 minutes after injection. Paired t-tests were utilized to determine

- 1) statistically significant differences between each time period compared to the control (baseline level before injection} for each anesthetic solution and
- 2) statistically significant differences between each solution at each time period.

Mean, standard deviation, mean difference (time period mean minus control mean}, and p-values are presented in Tables IV, V, and VI for systolic blood pressure and Tables VII, VIII, and IX for diastolic blood pressure.

Statistically significant increases in systolic blood pressure are noted at 45 minutes after injection without epinephrine (p<.035).

No statistically significant changes are noted in systolic blood pressure after injection with epinephrine nor are any significant changes noted in diastolic blood pressure with either drug.

No statistically significant differences between the drugs are noted for either systolic or diastolic blood pressure at any time period.

### Galvanic Skin Response

GSR was recorded continuously for all experiments on the twelve subjects. Results were analyzed by means of a paired t-test at 30 second intervals, starting one minute before injection (control) and

# TABLE IV

# SYSTOLIC BLOOD PRESSURE

## 2% Xy1ocaine without epinephrine



# \* Significant Values

# TABLE V

# . SYSTOLIC BLOOD PRESSURE

## 2% Xy1ocaine with epinephrine



# TABLE VI

# SYSTOLIC BLOOD PRESSURE

Comparison of 2% Xy1ocaine with or without epinephrine at different time intervals



# TABLE VII

# DIASTOLIC BLOOD PRESSURE

# 2% Xylocaine without epinephrine



# TABLE VIII

# DIASTOLIC BLOOD PRESSURE

## 2% Xy1ocaine with epinephrine



# TABLE IX

# DIASTOLIC BLOOD PRESSURE

## Comparison of 2% Xylocaine with or without epinephrine at different time intervals



continuing to 25 minutes after injection, to determine statistical differences in GSR between the two solutions. Mean difference, standard deviation, and p-values are presented in Table X.

The p-values show no significant differences in GSR as a result of these anesthetic solutions.

# TABLE X

# GALVANIC SKIN RESPONSE

Comparison of 2% Xylocaine with or without epinephrine at different time intervals



# TABLE X (cont.)



# TABLE X (cont.)



#### DISCUSSION

The results of this study show no statistically significant differences when comparing the effects of 2% xylocaine with or without epinephrine on heart rate, systolic, or diastolic blood pressures during pedodontic procedures. This is in agreement with several of the investigators cited in the literature review (Wallace et al., 1956, Cheraskin, 1958, and Elliot and Stein, 1974). They also agree with statements made by the New York Heart Association and in Accepted Dental Therapeutics. It must be mentioned, however, that no previous studies have used children as subjects.

Several investigators (Barcroft, 1949, McCarthy, 1957, and Allen et al., 1973), nevertheless, report decreases in diastolic blood pressure between 5 and 15 minutes after injection of an anesthetic solution with epinephrine. Figure I is a graph which relates all the parameters studied to each other on the same time scale. One can see a slight decrease, although statistically insignificant, in diastolic blood pressure at 15 minutes after injection with epinephrine. This decrease may or may not be related to the decrease reported by the aforementioned investigators.

Statistically significant decreases in heart rate during the later recording periods are evident in the results from both anesthetic solutions. These can be explained by the child's loss of apprehension to the dental situation.



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The significant increase in systolic blood pressure at 45 minutes after injection without epinephrine is probably attributed to the inefficiency and short duration of that solution.

The GSR results show no significant differences between the two solutions at any time period from 1 minute before injection to 25 minutes after injection. One must realize, however, that statistically significant results are difficult to obtain when the standard deviations are extremely large compared to the mean differences (Table X).

Figure I, however, demonstrates some definite trends for the GSR. The peak (without epinephrine) at 30 seconds presents the possibility that there is more discomfort associated with an injection without epinephrine. This could be due to the immediate vasoconstricting properties when using a solution with epinephrine, tending to keep more anesthetic in the general area during and immediately following the injection.

The curve without epinephrine remains more negative (thus, more stress, anxiety, or pain) from 6 minutes to 25 minutes. This can be explained by the reduced anesthetic efficiency of a solution without epinephrine (British Medical Journal, 1970; Gangarosa, 1967; and Bjorn and Hullet, 1947). In fact the peak at 15 minutes represents the need for reinjection of the solution without epinephrine which occurred in all but one case between 12 and 18 minutes after the original injection.

#### SUMMARY AND CONCLUSIONS

Twelve children aged 4 to 10 were monitored for heart rate, blood pressure, and galvanic skin response during dental procedures involving maxillary infiltrations with 2% xylocaine hydrochloride with and without 1:100,000 epinephrine. No statistically significant differences between the two solutions were noted  $5, 10, 15, 20, 30,$ and 45 minutes after injection for heart rate, systolic, or diastolic blood pressures.

The results from the GSR showed no significant differences between the two solutions due to the extremely large standard deviations encountered. However, certain observations and trends in the results tend to lead to the conclusion that the solution containing 1:100,000 epinephrine is more comfortable and effective than the solution without epinephrine when used for local dental anesthesia for children.

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#### APPROVAL SHEET

The thesis submitted by Robert A. Swanson, D.D.S., has been read and approved by the following committee:

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The final copies have been examined by the director of the thesis and the signature which appears below verifies the fact that any necessary changes have been incorporated and that the thesis is now given final approval by the Committee with reference to content and form.

The thesis is therefore accepted in partial fulfillment of the requirements for the degree of Master of Science in Oral Biology.

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