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# A Short-Term Histopathologic Study of the Effect of Gly-Oxide on Periapical Tissues in the Rhesus Monkey

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A SHORT-TERM HISTOPATHOLOGIC STUDY  
OF THE EFFECT OF GLY-OXIDE ON  
PERIAPICAL TISSUES IN THE RHESUS MONKEY

by

John William Gillan

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## DEDICATION

To my wife, Cindy, whose love makes my work worthwhile, and  
to my parents, whose support and love have led me to achieve this goal.

## VITA

The author, John William Gillan, is the son of John Howard Gillan and Mary Frances (George) Gillan. He was born February 13, 1948, in Oak Park, Illinois.

His secondary education was obtained at Pleasant Hill High School, Pleasant Hill, California, and then at Las Lomas High School, Walnut Creek, California, where he graduated in June, 1966.

In September, 1966, he entered the University of the Pacific, Stockton, California, where he graduated with honors in June, 1970, with the degree of Bachelor of Arts with a major in biological sciences.

In September, 1970, he entered Loyola University School of Dentistry, where he received the degree of Doctor of Dental Surgery in June, 1974.

In July, 1974, he began serving as a dentist for the United States Air Force at Williams Air Force Base in Arizona. He completed his military service in July, 1976.

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## INTRODUCTION

The problem of the pulpless tooth has been plaguing man for centuries. As long ago as the first century A.D., Archigenes trephined through periapical bone to relieve pain as a result of abscess formation(1).

Endodontics has been defined as that branch of dentistry concerned with the etiology, prevention, diagnosis, and treatment of diseases and injuries that affect the pulp and periapical tissues(2).

Such treatment was gaining favor in the profession until Rosenow reported (3) in 1930 that in persons ill with various chronic diseases, practically all pulpless teeth were infected. He proclaimed that devitalization of teeth and the filling of root canals as practiced in the past should cease. The problem with Rosenow's idea was that he determined teeth to be infected and the foci of systemic illness by extracting the teeth and incubating the entire tooth, which obviously would be contaminated from the oral fluids.

Since that time, endodontic therapy has been proven to eliminate the source of infection (4). Dentists and patients realize that proper root canal therapy supports restorative care by retaining strategic teeth. The purpose of endodontic treatment is to control residual infection within the root canal and maintain the integrity of the periapical tissues(5). Blechman and Schilder (6,7) stated that the objectives of root canal therapy extend beyond the root canal to apical and periapical tissues and all efforts should be directed to restoring and maintaining these tissues in optimum health.

Weine (8) divides root canal therapy into three phases:

1) the diagnostic phase; 2) the preparatory phase; and 3) obliteration or filling the prepared canal space. Most authorities agree that, by far, the most important phase is the chemomechanical preparation of the canal space. Irrigating solutions are considered to be indispensable aids in achieving thorough preparation by helping to gain debridement and disinfection of the canal. (9)

Endodontic treatment should thus enhance the repair of periapical tissues by the natural body defenses. This is achieved by removing the cause of irritation and avoiding the misuse of anything which might diminish the healing potential (10,11). Pain following endodontic instrumentation is due to periapical inflammation. During chemomechanical instrumentation, necrotic debris, dentin, pulp fragments, or irrigants may be forced into the periapical tissue. These materials may provoke an inflammatory reaction (12).

The use of Gly-Oxide \*, a urea peroxide in an anhydrous glycerol base, has been proposed by Weine (8) and Stewart (13) as a very useful root canal irrigant. Weine stated that it is better tolerated by periapical tissue than sodium hypochlorite, yet has greater solvent action and is more germicidal than aqueous hydrogen peroxide. Gly-Oxide is claimed, by the manufacturer, to be non-irritating and non-sensitizing (14). It is formulated to gently but thoroughly clean minor oral lesions so that normal healing can occur.

The purpose of this study is to evaluate the histological effects of Gly-Oxide on the periapical tissue when used as an endodontic irrigant.

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\* International Pharmaceutical Corp., Kansas City, Missouri 64114



## REVIEW OF THE LITERATURE

### History

Throughout recorded history, dentists have used various drugs and methods for treating diseased pulps. In the late 1800's, creosote, creosote and arsenic, nitrate of silver, and chloride of soda were used for cleaning out the root canals (15). Many other chemicals have been used over the years for irrigation of root canals. As early as 1864, investigators recognized that some of the root canal disinfectant drugs irritated the periapical tissues. The tendency at that time was to use the most powerful drugs for destroying the microorganisms within the root canal. Little attention was given to the effect produced in the surrounding periapical tissues (10).

### Intracanal Medication and Irrigation

Although their use and function are truly different, root canal irrigants are usually studied with intracanal medicaments.

Stewart (16) discussed the characteristics of an ideal root canal medicament:

1. It should be effective in eliminating or destroying those microorganisms which we normally find within the root canal.
2. It should destroy, or neutralize, or eliminate any toxic products which may be present within the root canal.

3. It should be non-irritating to healthy tissue and not produce toxic or allergic reactions.
4. It should not stain or discolor teeth.
5. It should have good penetrating qualities, in order to be effective deep within the dentinal tubules.
6. It should be stable at room temperatures.
7. It should not inactivate the natural defense mechanisms of the body.
8. It should not be inactivated by blood, or by serum protein or pus which may be present within the root canal or the periapical tissue.

In addition to these properties, Luebke (17) stated that irrigants must remove debris accumulated during canal debridement, remove necrotic organic material, and must wash out bacteria and destroy those susceptible to the irrigating agent.

#### Tissue Response to Medicaments and Irrigants

Boyle (18) stated that practically every drug used in a root canal causes at least slight periapical inflammation.

Blaney (19) mentioned that much harm has been done to the surrounding apical tissue by the use of coagulant drugs. He warned that one must be mindful of their effects on vital tissue.

Penick and Osetek (9) stated that the more effective an irrigant is as a necrotic tissue solvent, germicide, and bleaching agent, the less tolerable it will be to the tissues.

Morse (20) mentioned that some irrigants have been shown to act

as haptens, eliciting an antibody response. These irrigants included urea, sodium hypochlorite, and hydrogen peroxide. Considering the possibility, one should use the least allergenic and least inflammatory drug for irrigation and intracanal medication.

According to Schilder and Amsterdam (21), drugs can cause pain only if they are irritating per se, and then only if they are allowed to contact tissues which can be inflamed by them. While wholly desirable, limitation of instrumentation and irrigation within the confines of the canal cannot always be achieved. Schilder and Amsterdam tested aqueous hydrogen peroxide, three percent, in rabbits. Intradermally, there was no apparent inflammation. Moderate inflammation was evident in the conjunctival sac of rabbits. Sterile physiologic saline, which is non-irritating to the tissues, was used as a control. They stated that injudicious use of root canal medicaments and irrigants may be one of the factors responsible for post-treatment pain.

Guttuso (11) stated that the clinician has not always attached sufficient importance to the biologic assay of the material when seeking an efficacious root canal irrigant. Guttuso studied rat connective tissue responses to endodontic materials. He reported that it is imperative that the materials used in endodontics be compatible with living connective tissue in order to preclude any perverse response. If root canal medicaments or materials that are potentially irritating are injudiciously allowed to contact viable periapical connective tissue, pain associated with inflammation and necrosis may result. The chemical injury reduces the regenerative powers in the area, and optimal repair and function are lowered and success of treatment is less predictable. Previously estab-

lished periapical damage can be aggravated by the use of non-compatible irrigants.

Attala and Calvert (10) demonstrated an irritation potential of eight commonly used endodontic medicaments and irrigants when instilled into dogs' eyes and injected subcutaneously into guinea pigs. Aqueous hydrogen peroxide provoked a mild inflammatory reaction in guinea pig subcutaneous tissue. The authors summarized that endodontic drugs should be used with great care to minimize their extradental effect beyond the apical foramen.

Rickert and Dixon (22) in 1933, tested the tissue tolerance of various dental filling materials in rabbits. They did not employ periapical tissues in their tests.

Powell, Marshall, and Melfi (23) evaluated the histopathologic effect of various endodontic drugs by placing the drugs in polyethylene tubes on cotton and implanting the tubes into the subcutaneous connective tissue in the backs of rats. Empty tubes and saline-filled tubes served as controls. Formocresol produced the most severe reaction, but the tissue appeared histologically normal at 30 days.

Torneck (24) studied the reaction of hamster connective tissue to endodontic drugs. According to him, a minimum amount of injury elicited by a material will only alter the metabolism and function of cells to compensate for the irritant. If the irritation is more severe, complete cessation of all cellular activity and death of cells will result. Microscopic evidence of cellular injury is not always seen in the milder degrees of irritation.

Grossman (25) studied the irritating potential of root canal med-

icaments by placing the medicaments on the skin of the forearm for forty-eight hours. He tested one percent azochloramid, in triacetin, beechwood creosote, camphorated monochlorophenol, cresatin, and formocresol. Grossman pointed out that skin reaction is not synonymous with periapical reaction, and what happens on the skin surface may not occur when these medicaments come in contact with periapical tissue. It is very likely to be more irritating to the periapical tissue.

In another study, Attala (5) tested the effect of beechwood creosote and Chloramine on the periapical tissue of dogs. Creosote had a more severe reaction, showing infiltration of inflammatory cells in the apical periodontal membrane with an increase in collagen fiber bundles. Osteoclasts present in Howship's lacunae lining the areas of resorption were indicative of active bone resorption. Attala stated that it is imperative to avoid irritating chemicals which may lower the healing capacity of tissue.

Penick and Osetek (9) stated that strong caustic drugs are not needed for root canal medication or irrigation. If used, they frequently do more harm than good by producing periapical inflammation. Drugs used should have the lowest possible inflammatory potential consistent with the ability to maintain aseptic conditions within the canal. (26,27)

Some investigators (28,29) have tested the cytotoxic effect of various root canal medicaments on HeLa cell tissue cultures, which are epithelial cells isolated from cancer tissue. It is said to be justified to draw general conclusions from the results of these studies because the cytotoxic effect on HeLa cells would seem to be similar to that for normal cells.

Trowbridge (30) stated that cells with a high metabolic rate and

high oxygen requirement are more susceptible to injury by toxic chemicals than cells with a low metabolic rate. As an example, one would expect a dentinoblast in a developing tooth to sustain more damage from a cytotoxin than an undifferentiated mesenchymal cell or a fibroblast, in as much as the dentinoblast is more actively engaged in the synthesis of macromolecules.

Coolidge (31) was of the opinion that the drugs used for medication in root canals may be less harmful to the organism and to the health of the periapical tissue through chemical irritation than undestroyed microorganisms remaining in inaccessible places in the canal, which usually gain access to the periapical tissue after treatment and filling of the canal. In Coolidge's study of the reaction of dog tissue to root canal drugs, he desired to have the drug actually produce a reaction in order to observe and compare the results produced in a definite period of time.

Harrison and others (32) analyzed the clinical toxicity or pain realized from three irrigants: normal saline, 5.25% sodium hypochlorite, and a combination of three percent hydrogen peroxide and 5.25% sodium hypochlorite. Instrumentation was confined within the canal system and completed in one appointment. After final irrigation, the canal system was dried with paper points and the chamber was sealed. There was no significant difference in interappointment pain related to the type of irrigant used. Also, the study does not support the contention that using three percent hydrogen peroxide will cause pain in the periapical tissue (33,34). Harrison proposed that necrotic tissue debris remaining in the canal system after chemomechanical preparation may cause pain due to irritation of the periapical area.

Heuer (35) stated that the severity of the reaction to irrigating solution passing beyond the confines of the apical foramen is dependent on the volume injected, the toxicity of the solution itself, and the location of the periapical tissues.

Harris (36) reported a case of a severe complication of swelling and pain associated with the use of a dilute solution of sulfuric acid used to facilitate canal enlargement. He stated that harsh chemicals are very irritating to the periapical tissues when not confined to the canal. He suggested sodium hypochlorite or urea peroxide and sodium hypochlorite used alternately to cleanse canals and not harm the soft viable tissues periapically.

#### Chemomechanical Preparation

Several authors relate chemomechanical preparation of root canals to surgical preparation. Grossman (34) stated that an axiomatic principle of surgery is that before a wound is ready for chemotherapy, all necrotic material and debris must be removed. Dentists cannot ignore this principle in root canal therapy and rely principally on drug therapy.

Stewart and others (37,38) proclaimed that the elimination of inflamed or dead tissue, microorganisms, and toxic products, in order to encourage healing, serves the same purpose as wound debridement in surgery. They conceded that total debridement may not be possible, but it must be accomplished to a point within the physiologic limits of repair of the host organism. The more complete the removal of these irritants, the more complete the repair.

According to Masterton (39), adequate mechanical preparation of the root canals is a primary requirement in endodontics...and because of

the irregularity of root canals, chemical debridement is also advisable to ensure complete eradication of dead tissue and debris from the canal.

Kantz, Ferillo, and Zimmerman (28) mentioned that endodontists should rely more on the careful biomechanical cleansing of the root canal system rather than on the use of massive doses of toxic chemicals to eliminate microbial contamination.

Spangberg (40,41) stated in 1973 that in modern endodontics it is now generally believed that the effect of antiseptics in the treatment of diseases of the dental pulp and periapical tissues is overestimated and that if success is to be achieved, other factors must also receive adequate attention. He stated that infections are eliminated by mechanical cleansing of the canal facilitated by irrigation. The effect of irrigation can be increased by the addition of a surface active substance or a proteolytic substance to the fluid.

Careful selection and manipulation of irrigating solutions, combined with thorough but careful debridement and instrumentation, ensure the elimination of injurious agents from the root canal while preventing further irritation to the delicate periapical tissues. (9)

Matsumiya and Kitamura (42) stated that the thoroughness with which the enlarging and cleansing are performed is just as important as the choice of filling material in performing a successful treatment of infected root canals.

Heuer (43) recommended heavy irrigation before instrumentation to dilute the noxious fluids from the confines of the root canal.

Grossman and Meiman (44) in 1941 found that chlorinated soda was the most effective solvent of pulp tissue.

Chlorine irrigants have an advantage of being able to dissolve



organic debris. Schilder (7) stated that constant irrigation with mild germicidal chlorine solutions was often the only means of sterilizing inaccessible and unseen lateral canals.

Seltzer and others (45) stated that the use of irrigation following pulp extirpation and instrumentation for removal of debris or dissolution of pulp tissues is more readily tolerated by the periapical tissues when the irrigant is confined to the root canal.

Salzberger and Brilliant (46) evaluated, in vivo, the apical penetration of a radiopaque irrigating solution in root canals. Hypaque 50% (sodium diatrizoate) was used as the test irrigating solution. Sodium hypochlorite compares favorably in specific gravity and surface tension to the sodium diatrizoate solution. Extrusion of the irrigant occurred in cases with vital pulps and in cases with necrotic pulp tissue. Usually in most vital cases, the irrigant was confined to the instrumented space. In necrotic cases, the solution was not confined to the instrumented space, and occupied random dimensions when extruded into the periapical lesion.

Vande Visse and Brilliant (47) studied the effect of irrigation on the production of extruded material at the root apex during instrumentation. They found that more debris was extruded when irrigation was used as opposed to no irrigation.

Schilder (48) stated that irrigation must be abundant. Dentin shavings must be kept in loose suspension in the irrigating solution to prevent accumulation and compaction of dentin mud. Being on guard against the development of dentin mud at all times, half solves the problems created by its accumulation. Over a period of twenty patient visits for canal preparation, Schilder used an average of 39 cc. of sodium hypochlor-

ite per patient visit. It was accompanied in many cases by almost equal quantities of hydrogen peroxide.

Enlargement of the canal is far easier with an irrigant present, instrument breakage is reduced, and negotiation of the small canal is facilitated by the lubrication (9).

Senia and others (49) stated that irrigation is a must, especially to cleanse those areas of the canal system not reached by mechanical instrumentation. He reported that sodium hypochlorite did dissolve pulp tissue, but this action was questionable in the apical three millimeters of narrow root canals.

Grossman (33,34) was the first person to recommend using a combination of a reducing solution ( sodium hypochlorite) and an oxidizing solution ( hydrogen peroxide) used alternately -- producing greater cleansing effect by effervescence owing to the liberation of oxygen in its nascent state. The effervescence forces debris out of the canal. Grossman reported that the final irrigating medium must always be the sodium hypochlorite solution, since any hydrogen peroxide left in the canal may combine with a peroxidase of blood or organic material and release oxygen, thus causing pressure. Such pressure, when confined within a sealed root canal will cause swelling and pain of the periapical tissues (33,34). Harrison (32) disputed Grossman's theory.

Svec and Harrison (50) found that a combination of sodium hypochlorite and hydrogen peroxide was significantly more effective in cleansing the canal system one and three millimeters from the apex when compared to normal saline. At the five millimeter level, normal saline was equally effective as an irrigant. These authors also found that tissue debris

remained in the canal after chemomechanical preparation using either normal saline or a combination of three percent hydrogen peroxide and 5.25% sodium hypochlorite as irrigants.

Spangberg, Engstrom, and Langeland (41) also advocated the use of sodium hypochlorite as an irrigating solution for its proteolytic effect, but warned that irrigating solutions should not be tissue irritants because these solutions do contact vital tissue.

Heuer (43) found that the best penetration of dentinal tubules occurred when sodium hypochlorite was used with hydrogen peroxide. Acids and chelating agents reduced penetration below that of unirrigated canals.

Baker and others (51) assessed the effectiveness of several irrigating solutions utilizing the scanning electron microscope. They tested physiologic saline solution, hydrogen peroxide, sodium hypochlorite, hydrogen peroxide and sodium hypochlorite, Gly-Oxide, Gly-Oxide and sodium hypochlorite, and others. There seemed to be no apparent difference in the effectiveness of any of the tested solutions in removing root canal debris. There was 70% more debris in the unirrigated canals as compared with the irrigated canals. In their study, the irrigating solutions removed debris, but in varying amounts. The flushing action of the solutions, and not their tissue-dissolving qualities, appeared to be the significant factor. The use of greater volumes of solution seemed to produce better results than smaller volumes of the same solution. The length of time that the solution remained in the root canals did not significantly alter the results. Baker stated that, in general, one side of each root canal appeared more thoroughly debrided and cleaner than the opposite

side. Baker concluded that until a chemical solution that dissolves pulpal tissue and that is biologically compatible with periapical tissue is found, physiologic saline solution is probably the most biologically acceptable irrigating solution available.

In a scanning electron microscopic study of the efficacy of urea hydrochloride as an irrigating solution, Tucker and others (52) found significant amounts of tissue and debris remaining after instrumentation and irrigation of the canals.

Moodnik and others (53) found that even by irrigating after each instrument with saline or sodium hypochlorite, there was still a layer of sludge coating the instrumented walls.

Zurbruggen and others (54) utilized a radioisotope-labeled EDTA-urea peroxide carbowax glycerol compound for post instrumentation retention study. The amount remaining after thorough cleansing was almost four percent of that originally applied. The amount of residue did not decrease with reinstrumentation and irrigation.

#### Antimicrobial Effect

Spangberg (40) notes, when discussing intracanal medicaments, that even though an antimicrobial effect may, under certain circumstances, be desirable, the toxicity should be kept as low as possible in order to avoid injury to the tissues. The most suitable irrigating solution should thus have a maximal antimicrobial effect with minimal toxic effect. If the irrigating solution is used simply to facilitate mechanical cleansing and thus is not intended to have an antimicrobial effect, physiologic saline may be used.

Spangberg (40) discussed the role of antiseptic irrigants in the destruction of microorganisms within the canal. The oxidizing substances, namely chlorine and iodine compounds, as well as hydrogen peroxide, act by oxidizing the free sulfhydryl groups in the enzyme system of the bacterial cell wall. Spangberg also stated that sodium hypochlorite in 0.5% concentration has a good antimicrobial effect, low toxicity, and good cleansing action due to its proteolytic effect. He thus concluded that sodium hypochlorite, 0.5%, is a suitable irrigating solution for most types of endodontic treatment.

Schilder (7) in 1966 and Blaney (19) in 1928 reported that mechanical sterilization is accomplished by the physical removal of microorganisms and is as effective as their chemical destruction, and there is less chance of irritation from powerful antiseptics.

In 1953, Auerbach (55) demonstrated that by careful mechanical cleansing and irrigation of the canal alone, without the use of further medication, 78% of the infected teeth thus treated yielded growth-free cultures.

Later, Stewart (56) found that 76% of the infected teeth which were treated by chemomechanical preparation alone were free of microbial growth.

Ingle and Zeldow (57) found a great percentage of negative cultures following mechanical instrumentation alone.

Nicholls (58) and Sommer, Ostrander, and Crowley (59) also reported a large percentage of negative cultures with chemomechanical cleansing.

In testing the efficiency of sodium hypochlorite as an endodontic irrigant, Shih, Marshall, and Rosen (60) concluded that mechanical flush-

ing with sterile distilled water was much less effective in removing bacteria from the root canals than was the hypochlorite.

Akpata (61) explained that instrumentation and irrigation alone will not sterilize the root canal, but these procedures may significantly reduce the microbial population of the infected root canal such that negative cultures ensue.

Engstrom (62) agreed, stating that mere irrigation and cleaning of root canals with isotonic saline might reduce the bacterial flora at the initial test so much as to produce a false negative culture.

Grahnen and Krasse (63) tested the effect of instrumentation and flushing with various agents (saline, a quaternary ammonium compound, and a polyantibiotic). With regard to immediate clinical results, he found no obvious differences between the three groups. Bacteria were reduced in all groups.

Stewart and others (37) compared EDTA(ethylenediaminetetraacetic acid)-urea peroxide combination, aqueous hydrogen peroxide, and urea peroxide as irrigants for their antimicrobial efficacy. All gave very high percentages of growth-free cultures after the first treatment. The EDTA-urea peroxide mixture gave the best results at the second visit cultures.

## Healing

Muruzabal and Erasquin (64) discussed the process of healing following endodontic treatment, stating that inflammatory tissue reaction is a complex process depending not only on the irritating potential of the drugs used in the root canal, but also on the presence of tissue remnants. The inflammatory reaction is more severe where tissue remnants

are present and is important because a healing process cannot be considered biologically acceptable while persistent inflammatory cells adjoining the root canal are observed.

According to Stewart (56), if a tissue has the ability to heal, it will heal only if and when the irritants that prevent healing are reduced to within physiologic limits of repair. The rate and degree of healing will be directly proportionate to the reduction of irritation and the potential healing capacity of the tissue.

In 1927, Blaney (65) stated that the apical tissue has the power to repair the damage caused by the operation when the pulp is removed. He also stated that it is possible to remove a vital pulp and maintain healthy tissue, both within the apical ramifications of the canal and surrounding the root end.

In the presence of chronic irritation, granulation tissue forms. Kronfeld (66) relates that granulation tissue formation may be considered as the defensive or reparative reaction of the organism in as much as the granulation tissue initiates and precedes the healing of wounds.

According to Menkin (67), foreign substances, whether viable or not, in contact with otherwise normal tissue will induce an inflammatory reaction, the intensity of which may vary from a barely visible hyperemia to an intense suppurative process. The inflammatory response is a characteristic phenomenon common to all tissue.

#### Gly-Oxide and Urea Compounds

In 1961, Stewart and others (13) reported a study comparing Gly-Oxide with aqueous hydrogen peroxide in the chemomechanical preparation

of infected root canals in 77 single-rooted teeth. With both solutions, growth-free cultures were obtained in more than 90% of the cases after the initial cleansing and enlarging of the canal. However, with the initial culture at the second visit, Gly-Oxide was substantially more effective than the aqueous hydrogen peroxide in producing growth-free cultures.

Stewart, and Penick and Osetek (13,9) stated that the advantages of Gly-Oxide are improved antimicrobial action, stability at room temperatures, a slower liberation of oxygen when it contacts body fluids or infected material, and more prolonged action in this regard.

Gly-Oxide has other advantages during the preparation of the root canal. It acts as a lubricant for instruments, which is very helpful if the instruments are to be used in the very fine canals in mature teeth. When sodium hypochlorite is added, the effervescence helps to clean the canal (9). Aqueous hydrogen peroxide has a very rapid action, whereas the Gly-Oxide has a prolonged action which allows time to work the material down into the canals and to initiate the flushing action with the hypochlorite. In Stewart's study (13) there was no clinical evidence of irritation or allergic reactions produced by the Gly-Oxide.

Urea peroxide is a complex of hydrogen peroxide and urea and occurs as a white crystalline material with a slight odor. It is soluble in water, alcohol, glycerin, and propylene glycol. Urea peroxide gradually decomposes and should be kept from moisture, heat, and sunlight. Solid urea peroxide and its solutions in some non-aqueous solvents, such as glycerin are more stable than its aqueous solutions. Urea peroxide is incompatible with certain enzymes, metallic ions, and alkalies. (68)



Carbamide is another name for urea, which is a product of protein metabolism (69).

In 1936, Robinson (70) reported that urea had been found to stimulate healing in chronic purulent wounds. The effects obtained were a cleansing of the wound by the removal of necrotic material and pyogenic bacteria, and a promotion of the growth of granulation tissue.

In 1953, Blechman (6) discussed urea as a root canal irrigant. He remarked that urea in strong solution has a strong solvent effect upon denatured proteins-- necrotic tissue, pus and debris. It is innocuous to vital tissues and during its use the processes of repair are not retarded. Blechman said that urea is bland and non-irritating to tissue, and deodorizes putrescent suppurating canals.

In 1946, Brown and others (71) discussed urea peroxide. They stated that saliva catalyzed the breakdown of aqueous peroxide to a much greater extent than with the polyhydric alcohol (glycerol) solutions of urea peroxide. Brown stated that the ideal antiseptic for topical application: 1) must be stable, non-toxic, non-irritating, and non-allergenic; 2) must act fairly quickly yet its actions in mixed infections must be relatively long lasting and effective; and 3) its properties should permit its safe application to tissues. Brown discovered that the urea peroxide could be stabilized in alcohols and especially glycerol.

Cobe and associates (72) studied the antimicrobial effect of Gly-Oxide as compared to aqueous hydrogen peroxide in the presence of blood. They found that Gly-Oxide has a much slower rate of reaction with citrated human blood than does aqueous hydrogen peroxide. The longer the period of oxygen release, the greater the chance of bactericidal action

to take place.

Baker (51) studied the efficacy of several irrigating solutions, including Gly-Oxide, and found that there was no apparent difference in their ability to cleanse the canal walls.

Cobe and others (73) studied the value of Gly-Oxide, as an adjunct to periodontal therapy. They found that the residual urea exerted its known action in promoting wound healing and in neutralizing an acid environment. Cobe also stated that urea peroxide in glycerol is of value in maintaining an environment conducive to health after periodontal scaling and curettage.

Epstein (74) showed that urea peroxide in glycerin is an aid in controlling the severity of gingival inflammation in the general population.

Arefian (75) tested the vital tissue tolerance of several root canal medicaments, including Gly-Oxide. The material was injected into the subcutaneous tissue of rats. In the Gly-Oxide specimens the skin appeared hyperemic after six hours. By the sixth day a scab had replaced the hyperemic area. Histologic appearance of the irritation was rated as mild, moderate, or severe. Gly-Oxide and aqueous hydrogen peroxide both were rated as causing moderate reactions, as compared to the mild reactions of camphorated monochlorophenol, cresatin, and eugenol. Formocresol elicited a severe reaction.

There have been no periapical studies of the effects of Gly-Oxide used as an irrigant. The present study is designed to determine the periapical reaction to Gly-Oxide.

## MATERIALS AND METHODS

Two adult Rhesus monkeys (Macaca mullata) were used as experimental models to study the short-term periapical tissue reaction to intracanal irrigation with Gly-Oxide. Specimens representing post-operative intervals of one, seven, fourteen, and 30 days were obtained for microscopic evaluation. The animals were treated and housed at the Loyola University Medical Center Animal Research Facility. They were individually caged and fed a diet of standard laboratory chow, fresh fruit, and water ad libitum.

Following a quarantine period of at least thirty days, the monkeys' chests were shaved and a dye tattoo number was placed on the exposed area. The numbers tattooed on the monkeys were 2721, which will be referred to as monkey #I, and 2723, which will be referred to as monkey #II.

During the first session with the monkeys, their weights were recorded, and they were examined clinically and radiographically to rule out any oral abnormalities. The maxillary arch of monkey #I was utilized for the 30 day specimens; the mandibular arch of monkey #I for the seven day specimens; the mandibular arch of monkey #II for the fourteen day specimens and the maxillary arch of monkey #II for the one day specimens.

In order to work with the monkeys, prior to each experimental session, the monkey was given 0.6 cc of Sernylan (phencyclidine hydrochloride)\* intramuscularly. Sernylan is a central nervous system depressant.

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\* Bio-Ceutic Laboratories, Inc., St. Louis, Mo.

Atrosed (atropine sulfate)\* was administered one cc subcutaneous-ly at the same time that the Sernylan was given. Atrosed is a cholinergic blocking agent. The action of the drug is to stimulate the respiratory mechanism and to decrease the flow of saliva to facilitate the operative conditions.

Sodium phenobarbital \*\* was administered intravenously to induce surgical anesthesia for the dental procedures. Sodium phenobarbital is a barbiturate which acts at the cortical level of the central nervous system. Anesthesia was attained prior to the initiation of the experimental procedures. Venipuncture was made on the dorsal surface of the lower leg and an initial dose of 0.5 cc/Kg of the barbiturate was given. Monkey #I weighed approximately seven kilograms and monkey #II weighed approximately five and a half kilograms.

Twenty canals in twelve teeth were treated chemomechanically in each animal. One tooth per monkey was used as an absolute control, not being opened at all for instrumentation. The canals of three teeth were prepared in each quadrant: the lateral incisor and the first and second premolars. The operative field was kept as surgically clean as possible. Standard incisal or occlusal access preparations were made with a #701 bur in a high speed handpiece. Estimated working lengths were obtained from the preoperative radiographs. Final working lengths were obtained by radiographing the teeth with #10 type K Star files \*\*\*placed in the

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\*Burns-Biotec Laboratories, Oakland, California

\*\*W.A. Butler Company, Columbus, Ohio

\*\*\*Star Dental Mfg. Company, Conshohocken, Pennsylvania

canals. In order to maintain the established working length, silicone rubber stops were set at the proper length on the files. Great care was taken to maintain the proper working length during canal preparation so that inflammation would not be caused by passage of the instrument beyond the apical foramen. Ideally, the instrumentation was kept one millimeter short of the radiographic apex to ensure expulsion of the irrigant into the periapical tissues. The control teeth were irrigated with sterile physiologic saline. Saline has been reported as being innocuous to tissues and, therefore, serves as an excellent basis for comparison. The experimental teeth were irrigated with Gly-Oxide\*. During instrumentation, the canals were constantly flooded and flushed with the respective irrigating solutions, as is the routine procedure in root canal preparation. Irrigating and flushing of the canal debris was facilitated by the use of the combination irrigation-suction device originally described by Kahn and co-workers (76).

The canals were instrumented until clean, white dentinal shavings appeared along the length of the file. In most canals, the final instrument was a #30 or #35 file. After the final instrument was withdrawn, the canals were heavily irrigated. The canal orifice and chamber were dried with cotton pellets, fresh cotton was placed over the openings, and a double seal of zinc oxide and eugenol followed by amalgam was placed to seal the access opening.

The number of teeth instrumented and irrigated in each operating time is given in Table 1.

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\* International Pharmaceuticals, Inc., Kansas City, Mo.

A total of twelve teeth were irrigated with saline and an equal number with Gly-Oxide.

The monkeys were sacrificed to obtain one, seven, fourteen, and 30 day post-operative specimens. Sacrifice was accomplished by IV injection of Beuthanasia-D \*, a concentrated solution of sodium pentobarbital. Approximately seven to ten milliliters were injected. Death occurred within fifteen seconds after injection. The maxillary and mandibular arches were resected and radiographed. After removal of soft tissue, the cortical plate was thinned with a bur in a high speed handpiece to permit better tissue fixation. The access cavity seals were also removed to allow the fixative to enter the root canals. The specimens were placed in ten percent neutral buffered formalin for three weeks. The specimens were then removed from the formalin, washed in water and placed in a solution of equal parts of 45% formic acid and 20% sodium citrate for decalcification. The decalcification took approximately four weeks. Extraneous tissue was removed to provide convenient blocks of the appropriate size for histologic sectioning. These blocks were embedded in paraffin and cut to provide six micron sections. The sections were stained alternately with hematoxylin and eosin and Masson's trichrome connective tissue stain.

The histologic sections were studied under a light microscope, using magnifications of 100 and 400 diameters.

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\* Burns-Biotec Laboratories, Oakland, California

## RESULTS

Pre-operative clinical examination of the animals revealed no oral abnormalities and all experimental and control teeth utilized in this study were caries-free and normal, periapically, as determined by radiographic examination prior to operation.

The histologic appearance of the pulp of the unoperated control teeth was within normal limits (Fig. 1). The peripheral walls of the pulp canal were lined with mononuclear dentinoblasts. Adjacent to the dentinoblasts, the eosinophilic, light-staining predentinal region could be seen. Beneath the dentinoblastic layer the cell poor zone or the zone of Weil was noted. Capillaries and nerves were observed in this area. Proceeding centrally, the next distinct area of the pulp was the cell rich zone. Fibroblasts were the most commonly seen cell throughout this zone. They were seen associated with collagen fibers throughout the stroma of the pulp. There was a greater concentration of fibroblasts coronally than apically. On the other hand, there was more collagen apically, with a less dense arrangement of collagen fibers seen coronally. Pericytes could be seen associated with the thin walls of the capillaries. The central zone of the pulp contained fibroblasts, larger blood vessels, and larger myelinated nerves(8).

The periodontal ligament was composed mainly of densely arranged collagen fiber bundles (Fig. 2) The attachment of the fibers to the bone and to the cementum (Sharpey's fibers) could be seen in the prepared sections. At the apex of the tooth, the fibers seemed to run somewhat

parallel to the apical cementum. Fibroblasts were the most common cell in the periodontal ligament. Cell rests of Malassez, which appeared as oval groupings of epithelial cells, were evident at various points along the periodontal ligament. Peripheral to the alveolar bone were large groupings of fat globules representing normal fatty marrow.

The instrumentation of the experimental teeth, in which Gly-Oxide or physiologic saline were used, was not always as complete as was desired. The root canals of most specimens showed evidence of instrumentation to within one millimeter of the apex. Dentin filings and tissue debris were observed in almost every instrumented specimen.

#### One day specimens -- Gly-Oxide (Fig. 3,4)

In the one day specimens irrigated with Gly-Oxide, there were scattered polymorphonuclear leukocytes in the apical portion of the prepared canal space. Intact tissue was present along one side of the canal, showing dentinoblasts lining portions of the canal wall. In some sections, the periapical region showed no signs of inflammatory reaction. Fiber bundles appeared normal, with capillaries coursing through the periapical tissues. In the sections exhibiting a reaction, acute inflammatory cells were present at the exit of the apical foramen, both within the root canal and in the adjacent periapical tissue.

#### One day specimens -- Saline (Fig. 5,6)

The readable sections of the one day specimens that were irrigated with normal physiologic saline showed uninstrumented tissue mainly on one side of the canal. Intact dentinoblasts, adjacent to the predentin layer were visible and looked the same as with the one day Gly-Oxide specimens.



Many polymorphonuclear leukocytes were visible near the apical foramen in the periodontal ligament. The area adjacent to the foramen was also infiltrated by a small number of mononuclear lymphocytes. Many acute inflammatory cells were located in some of the adjacent periapical marrow spaces. (Table 2)

#### Seven days specimens -- Gly- Oxide (Fig. 7,8)

In the seven days specimens irrigated with Gly-Oxide, a mild inflammatory periapical response was evident. Clastic cells were present within resorption lacunae in both periapical bone and periforaminal cementum. There was a chronic inflammatory infiltrate of lymphocytes and plasma cells in the apical periodontal ligament. The vasculature was still not apparent, as was the case in the periodontium of the unoperated controls.

#### Seven days specimens -- Saline

The saline irrigated specimens showed mild chronic inflammation, periapically, seven days after initial treatment. There was a visible but sparse population of lymphocytes and plasma cells with a few polymorphonuclear leukocytes present. Multinucleated clastic cells were present in lacunae in the bone near the apical foramen and in the apical cementum. There were large vessels coursing through the apical periodontium. ( Table 3)

#### Fourteen days specimens -- Gly-Oxide

The histologic sections of the teeth irrigated with Gly-Oxide fourteen days before sacrifice were all poorly prepared, and could not be evaluated microscopically.

## Fourteen days specimens -- Saline

Only one tooth from the fourteen day saline specimens showed intact periapical structures , and could be evaluated. The periodontal tissue displayed no inflammatory reaction. The root canal contained a considerable amount of residual tissue and debris, thereby rendering the periapical response invalid with respect to the effect from the irrigant alone.

## 30 days specimens -- Gly-Oxide (Fig. 9)

The 30 days Gly-Oxide specimens showed healing granulation tissue. Polymorphonuclear leukocytes were aggregated in the apical portion of the prepared canal space. The canal contained scattered dentinal shavings. Large, young osteoblasts surrounded the osseous trabeculae adjacent to the root apex. There were many plasma cells and lymphocytes in the periapical tissue. There were some isolated areas of minor bone resorption with osteoclasts in Howship's lacunae. In one specimen, intracanal resorption was seen in one small area of the canal near the apex.

## 30 days specimens -- Saline (Fig. 10,11,12,13)

In the canals irrigated with physiologic saline 30 days prior to sacrifice, there was a varied periapical reaction. The canal in the lateral incisor was not prepared sufficiently to the apex, and results were consequently invalid for this specimen. Lymphocytes and plasma cells were visible in moderate amounts in the apical tissues and their numbers predominated over those of the neutrophils. Lymphocytes were especially abundant. There was severe active bone resorption in the apical osseous tissues. Much of the bone was lined with osteoclasts in lacunae, and

some active cemental resorption was also seen. One block section showed a healing granuloma. Lymphocytes and plasma cells were present. The granuloma was surrounded by a fibrous connective tissue capsule. New bone formation was apparent with osteoblasts lining the osseous tissue. (Table 4).

## DISCUSSION

The basic objective of root canal therapy is to tip the scales in favor the natural defensive and healing mechanisms of the body. Hartwell (77) discussed the healing of wounds, and stated the histologic findings in human wounds healing by primary intention differed markedly from those of similar wounds in laboratory animals. However, Hartwell's discussion only concerned surface connective tissue healing. Due to moral and legal constraints, human experimentation with respect to the potential effects of drugs and medicaments on tissue cannot be performed. Hence, animals must be used as experimental models in such studies, especially since block sections of tissue are often needed for histologic evaluation in these investigations.

Sample size is an important consideration in drawing conclusions in any scientific investigation. In the present study, the sample size was quite small to begin with, and unforeseen circumstances that occurred during the actual experiment decreased sample size even further. Due to errors in preparation, the histologic sections from the fourteen day specimens could not be evaluated. Some of the specimens from the other experimental time periods also could not be evaluated. However, most were acceptable.

Several sections revealed intact tissue and debris remaining in portions of the instrumented canals. It is well documented(49,50,52,78) that tissue debris remains despite the best attempts at canal instrumentation.

One of the findings in this study was the presence of an acute inflammatory infiltrate (polymorphonuclear leukocytes) associated with the residual tissue debris, thus indicating its noxious potential. The cytolytic enzymes released from devitalized tissue diffuse periapically and thus, stimulate extraradicular inflammation both in the canal and periapically. The tissue debris may also serve as a nutritive substrate for microbial growth within the canal, thus potentiating the irritation to the periapical tissues.

Inflammation was evident after irrigation with both Gly-Oxide and physiologic saline. Whenever tissue is irritated or destroyed, inflammation is the immediate protective response (79). The inflammatory response destroys, dilutes or walls off the injurious agent and the damaged tissue cells that these agents may have injured. Although the events of the inflammatory response follow a regular progression and occur in a predictable sequence, the ultimate character, extent and severity of the tissue changes are modified by factors related to both the host and the destructive agent. The protective events of inflammation in order of manifestation are:

- 1) Arteriolar dilatation, sometimes preceded by a transient vasoconstriction.
- 2) Increased rate of blood flow through the arterioles, capillaries and venules.
- 3) Capillary and venular dilatation and increased permeability. (In the present study, the vasculature was more pronounced in some specimens than others.
- 4) Exudation of fluid (outpouring of inflammatory fluid

through an injured membrane), including all the proteins of the plasma (albumin, globulin, and fibrinogen).

- 5) Concentration or packing of red blood cells in the capillaries.
- 6) Slowing or stasis of the blood flow.
- 7) peripheral orientation of the white cells in the capillaries (margination).
- 8) Migration of white cells from vessels into the inflammatory focus (diapedesis)-- polymorphonuclear leukocytes (neutrophils), first, followed by monocytes, lymphocytes, and plasma cells later.

In the well defined acute inflammatory stage, the neutrophils are the dominant cells, although other types of white cells, such as macrophages and scattered lymphocytes, may also be present. Acute response is also described as an exudative response since there is vascular congestion and exudation of fluids and white cells. After the irritant has persisted for days, the response is of the chronic or proliferative nature, showing an increase in fibroblasts and vasculature. Although the predominant cellular exudate is mononuclear, neutrophils may still continue to be present. The neutrophils are commonly present in the central zone of the chronic reaction, surrounded by endothelial and fibroblastic proliferation and a mononuclear cell reaction of lymphocytes, plasma cells, and macrophages. The macrophages, like the neutrophils, function in the phagocytosis of foreign material.

Rutberg, et al (80) discussed the acute inflammatory response and its enhancement of vascular permeability. He stated that the change in the vessel walls is almost instantaneous after an insult and may vary

with the nature of the irritant. Leakage may be due to direct damage to the blood vessels and also to the release of chemical mediators, such as histamine, from the host tissue. Increased vascular permeability is reflected by the passage of plasma proteins out of the vessels into the extravascular tissue. In this study, Rutberg used dyes that attached to plasma proteins.

In the specimens instrumented and irrigated one day before sacrifice, the periapical reaction appeared similar regardless of whether Gly-Oxide or saline was employed as the irrigant. The specimens exhibited a mild acute inflammatory infiltrate consisting of polymorphonuclear leukocytes. Occasional cells of the chronic inflammatory series were seen associated with the saline treated specimens, but their numbers were generally insignificant. As mentioned previously, lymphocytes are often present along with neutrophils during the initial response, but in lower numbers.

The seven day specimens treated with both irrigants exhibited similar histologic pictures. Mild chronic inflammation was evident in the periodontium of both groups. There was some clastic activity, indicating active resorption of the bone and cementum.

Chronic inflammatory reactions were seen in both of the 30 day experimental groups. The saline group showed a more destructive inflammatory response than the Gly-Oxide specimens, but the saline group also had one block showing a repairing granuloma, with newly formed osseous tissue adjacent to mature bone. In some of the saline specimens, the periapical bone was lined with resorption lacunae harboring multinucleated giant cells.

Seltzer (12) reported that weeks after the completion of canal

preparation, granulation tissue was found in the apical-periapical tissue complex. He stated that the granulation tissue constituted a defense reaction to the irritation caused by the pulpal extirpation and canal instrumentation, and was a precursor to repair. Granulation tissue is rich in macrophages, lymphocytes, and plasma cells. Neutrophils, in lesser concentrations, are also present. Granulation tissue consists of new capillaries, surrounded by mesenchymal cells. At the periphery of a healing granuloma, osteoblasts appear and new bone is elaborated. Immediately subjacent to the osteoblasts is a thin layer of pale-staining "osteoid".

In 1940, Englander (81) reported that periapical bone will regenerate after proper root canal cleansing and filling.

There are shortcomings in this study which limit the validity of any conclusions with regard to the tissue response to Gly-Oxide as compared to that with normal physiologic saline. As mentioned previously, some canals were not instrumented adequately, leaving tissue and debris in the canal space. Thus, it cannot be stated that the periapical inflammatory reaction was totally due to the irrigant alone. In the past, controversy has existed as to whether a root canal could be left unfilled subsequent to canal preparation. In the 1930's, Rickert and Dixon (82) implanted hollow tubes made from platinum and steel hypodermic needles (1 cm. or more in length) into the subcutaneous tissue of rabbits. They reported that macroscopically, the implants showed a large halo of irritation around the open tube ends while adjacent to the middle portions of the tubes, which were closed, the tissue was essentially uninfamed. Without the use of histologic sections, Rickert and Dixon concluded that there was a diffusion of stagnant circulatory substances out of the open



ends of the tubes and that these substances were not well tolerated by the adjacent vital tissue.

In 1966, Torneck (83) studied rat connective tissue microscopically, after surgically implanting hollow polyethylene tubes subcutaneously. He concluded that the tissue surrounding the lumina was relatively free of inflammation and displayed a normal capacity for repair.

Phillips (84) also reported a histologic study which failed to confirm the work of Rickert and Dixon. The study was similar to that of Torneck's. No inflammatory response was found at the open ends of any of the implanted tubes. All of the tubes were encapsulated by fibrous connective tissue.

Davis, Joseph, and Bucher (85) tested the hollow tube concept by utilizing widely prepared, underfilled root canals in dog teeth. Periapical healing around the underfilled canals in the dogs compared favorably to that around canals instrumented and filled to the apex, provided that the underfilled canals were prepared to the apex.

Relating the present study to the hollow tube theory, the presence of residual intracanal tissue debris was probably more significant as a source of periapical inflammation than the canals being unfilled. Considering the mild reaction exhibited by the one day specimens, it is likely that had all canals been completely cleansed of tissue, the periapical reaction seen at the longer post-operative periods would have been minimal.

The reason that this study consisted entirely of short term specimens is because most root canal therapy is performed within one month's time.

## SUMMARY

While following established endodontic procedures, the root canals of two rhesus Macaca mullata monkeys were instrumented and prepared to within one millimeter of the radiographic apex. The canals were irrigated constantly with either Gly-Oxide or normal physiologic saline.

Specimens representing post-operative intervals of one, seven, fourteen, and 30 days were obtained for microscopic investigation. Block sections were taken following sacrifice, and histologic sections were prepared using hematoxylin and eosin, and Masson's trichrome stains. The sections were studied and observations were recorded. Comparative histopathologic evaluations were noted between the effects of Gly-Oxide and the effects of saline on the periapical tissue.

## CONCLUSIONS

Under the conditions of this study, certain conclusions can be drawn:

- 1) It is not possible to remove all tissue debris from the canal, even with constant irrigation.
- 2) The tissue debris remaining in the prepared root canal appeared to be a source of periapical irritation resulting in inflammation.
- 3) There is no significant difference between the effect of Gly-Oxide and normal physiologic saline on the tissue.

Further studies of a similar nature should be done to compare periapical responses to irrigation with saline; Gly-Oxide; sodium hypochlorite

and sodium hypochlorite followed by Gly-Oxide.

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APPENDIX

## Abbreviations for Tables and Figures

A	=	Root Apex
ab	=	Alveolar Bone
ABR	=	Alveolar Bone Resorption
c	=	Canal
CIC	=	Chronic Inflammatory Cells
CR	=	Cementum Resorption
CT	=	Connective Tissue
D	=	Dentin
db	=	Dentinoblastic Cells
f	=	Foramen
fc	=	Fibrous Capsule
g	=	Granulation Tissue
MCI	=	Mild Chronic Inflammation
Ob	=	Osteoblast
Oc	=	Osteoclast
PDL	=	Periodontal Ligament
PMN	=	Polymorphonuclear Leukocytes
pt	=	Pulp Tissue
td	=	Tissue Debris

Table 1

## Number of Specimens

Days	Irrigant	
	Saline No. of Teeth	Gly-Oxide No. of Teeth
1	3	3
7	3	3
14	3	3
30	3	3

Table 2

## One Day

Irrigant	Gly-Oxide	Saline
Periapical Tissue	Scattered PMN in foramen and adjacent PDL.	PMN next to foramen. Few CIC in adjacent PDL.

Table 3

## Seven Days

Irrigant	Gly-Oxide	Saline
Periapical Tissue	Little ABR; CR; MCI and CIC in PDL. Vessels not apparent in PDL.	MCI Sparse CIC and PMN. Vessels in PDL.

Table 4

30 Days

Irrigant	Gly-Oxide	Saline
Periapical Tissue	Granulation tissue. Isolated areas of minor ABR. Many CIC in PDL. Much osteoblastic activity.	Moderate CIC. Sparse PMN. Moderate CR. Fibrous CT capsule. One specimen--severe ABR. Osteoblastic activity.

Fig. 1 Normal, uninstrumented root canal showing normal pulp tissue (pt) with dentinoblastic cell (db) lining; Dentin (D); Hematoxylin and eosin stain. X40.

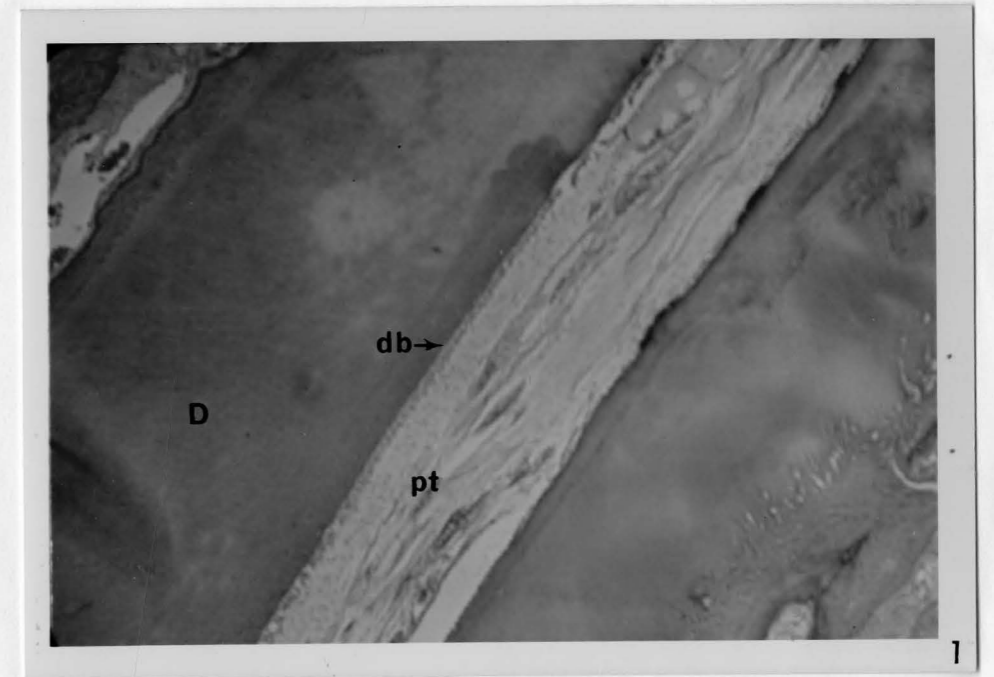


Fig. 2 Normal, uninstrumented tooth showing normal root apex (A) and periodontal ligament (PDL); dentin (D); alveolar bone (ab); Hematoxylin and eosin stain. X25.

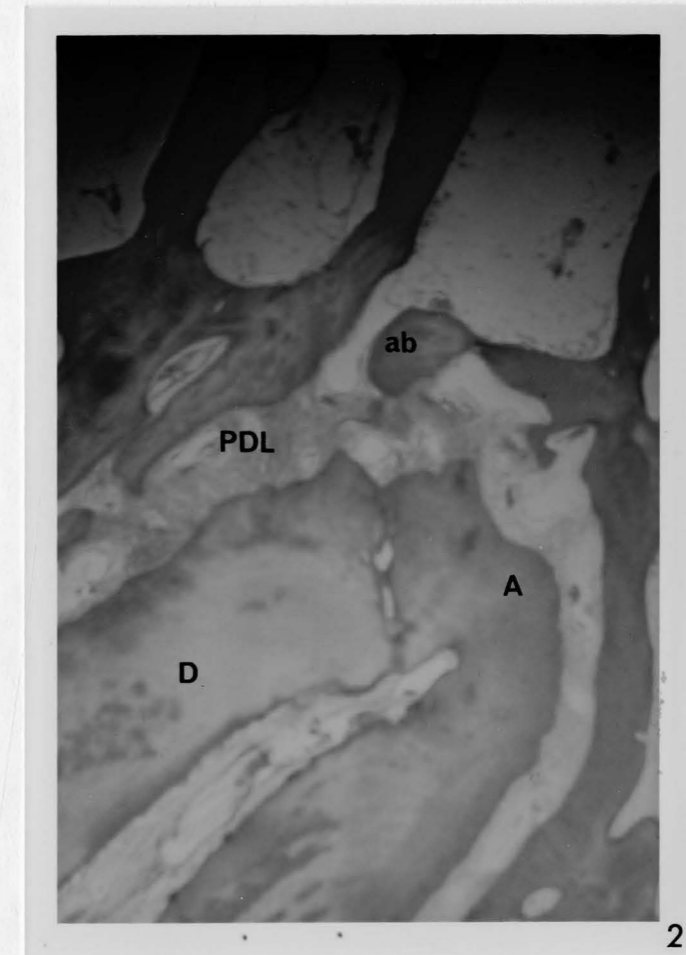
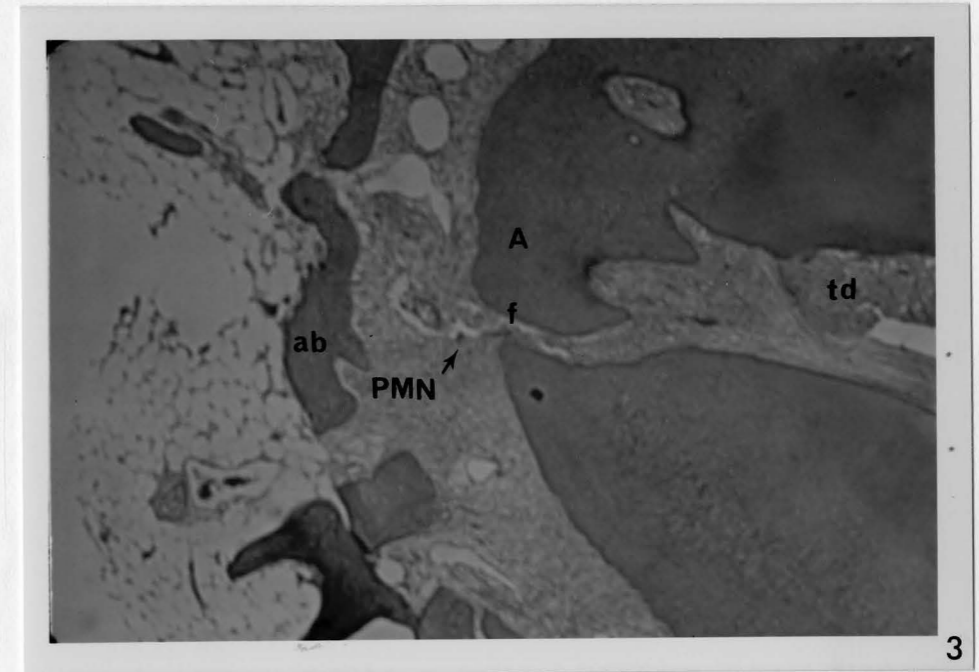


Fig. 3 One day specimen irrigated with Gly-Oxide; Tissue debris (td) within canal; Polymorphonuclear leukocytes (PMN) congregated near apical foramen (f); Alveolar bone (ab); Hematoxylin and eosin stain; X40.



3

Fig. 4 One day specimen irrigated with Gly-Oxide; Apical foramen (f) filled with tissue and inflammatory cells (PMN); root apex (A); Alveolar bone (ab); Hematoxylin and eosin stain; X100.



4



Fig. 5 One day specimen irrigated with saline; Tissue debris (td) within canal; Polymorphonuclear leukocytes (PMN) at foramen and in periodontal ligament; Root apex (A); Masson's tri-chrome stain; X25.



Fig. 6 One day specimen irrigated with saline; Polymorphonuclear leukocytes (PMN) congregated at the root apex (A); Tissue debris (td) in canal; Hematoxylin and eosin stain; X100.

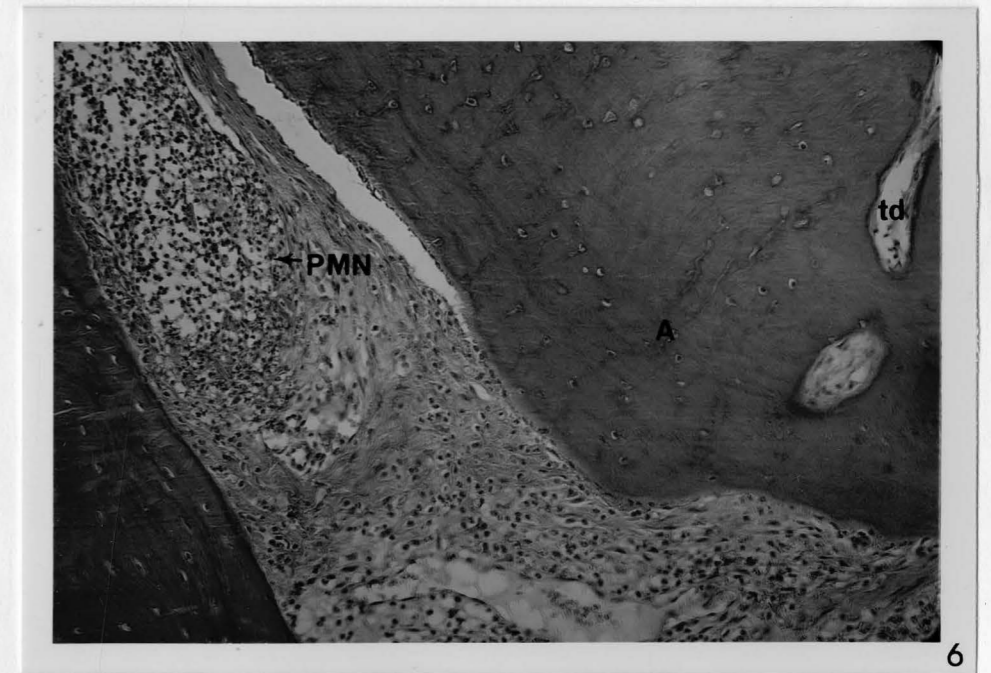


Fig. 7 Seven day specimen irrigated with Gly-Oxide; Osteoclasts (Oc) present in periapical alveolar bone (ab); Masson's Trichrome stain; X100.

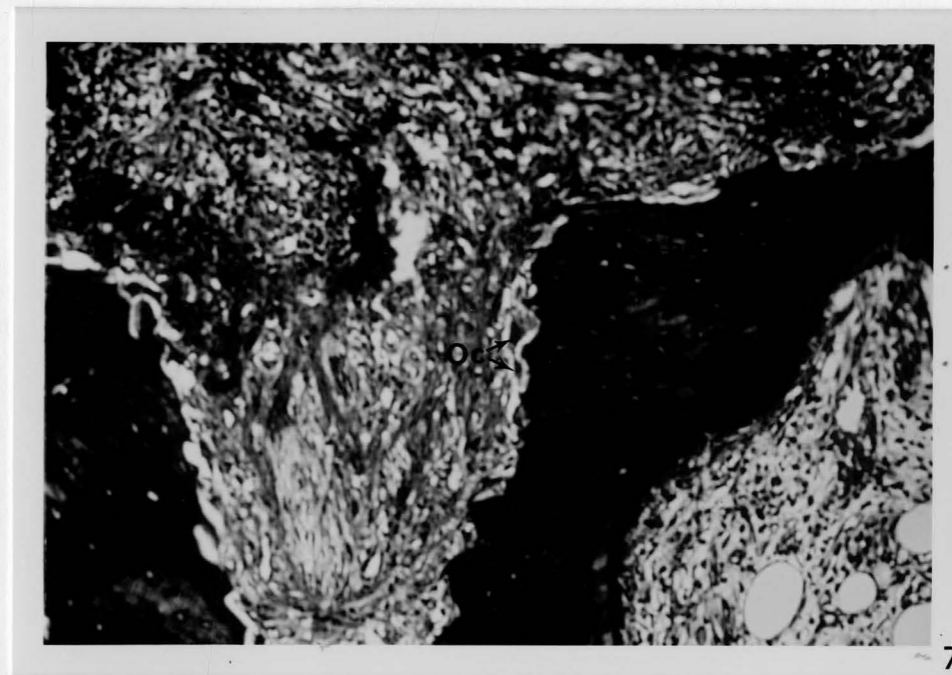


Fig. 8 Seven day specimen irrigated with Gly-Oxide; Avascular periodontal ligament (PDL); Osteoclasts (Oc) present in bone adjacent to root apex (A); Canal (c); Hematoxylin and eosin stain; X40.

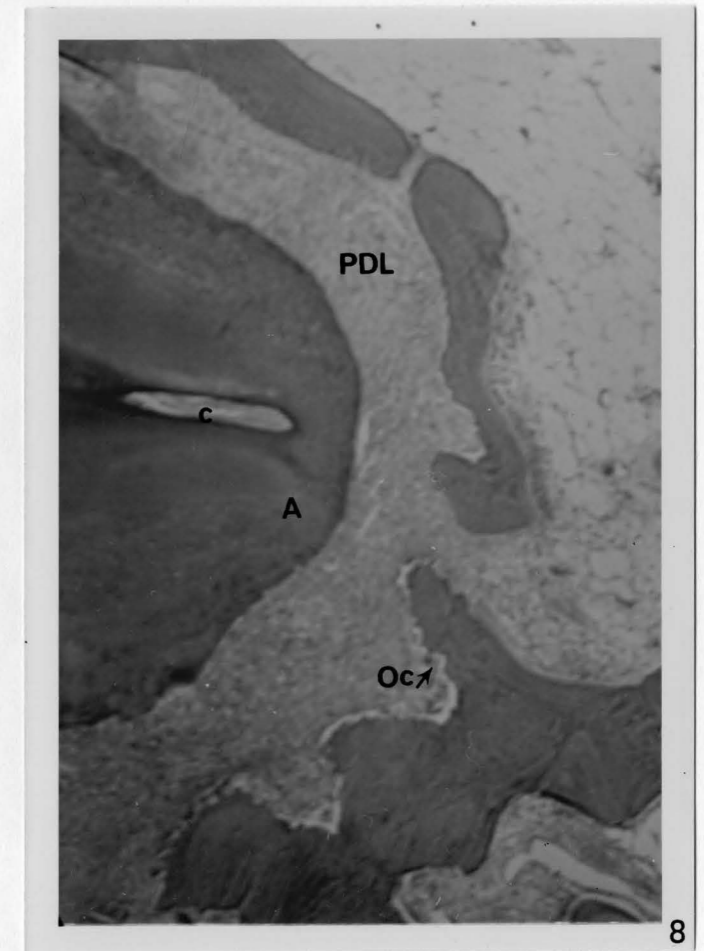


Fig. 9 Thirty day specimen irrigated with Gly-Oxide; Chronic inflammatory cells (CIC) adjacent to root apex (A); Tissue debris (td) present in canal space; Young osteoblasts (Ob) surround apical bone; Hematoxylin and eosin stain; X40.

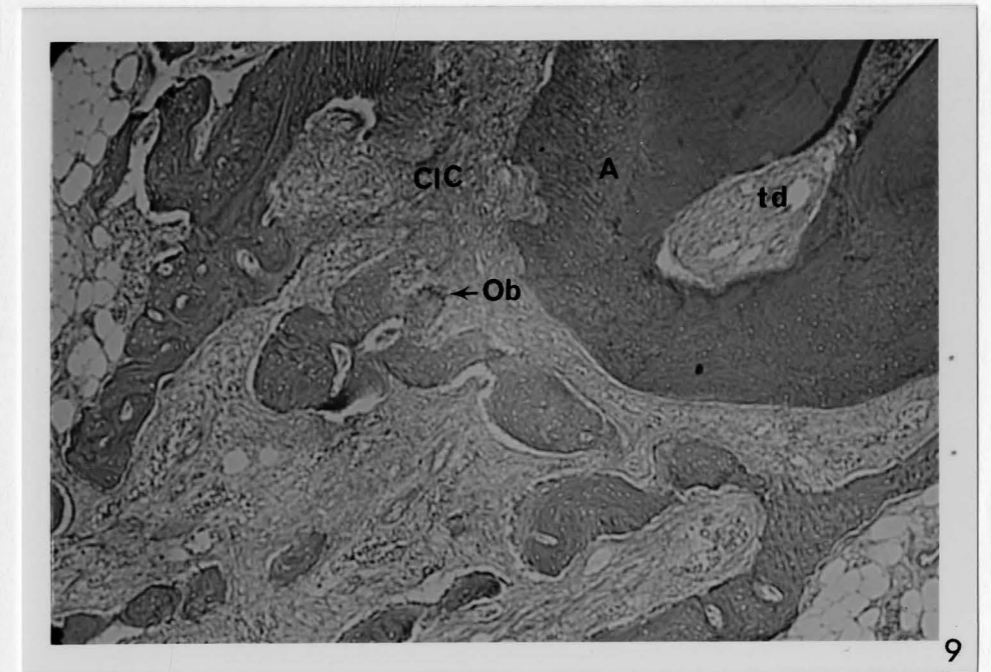


Fig. 10 Thirty day specimen irrigated with saline; Granulation tissue (g) next to root apex; Osteoblasts (Ob) forming new bone; Hematoxylin and eosin stain; X40.

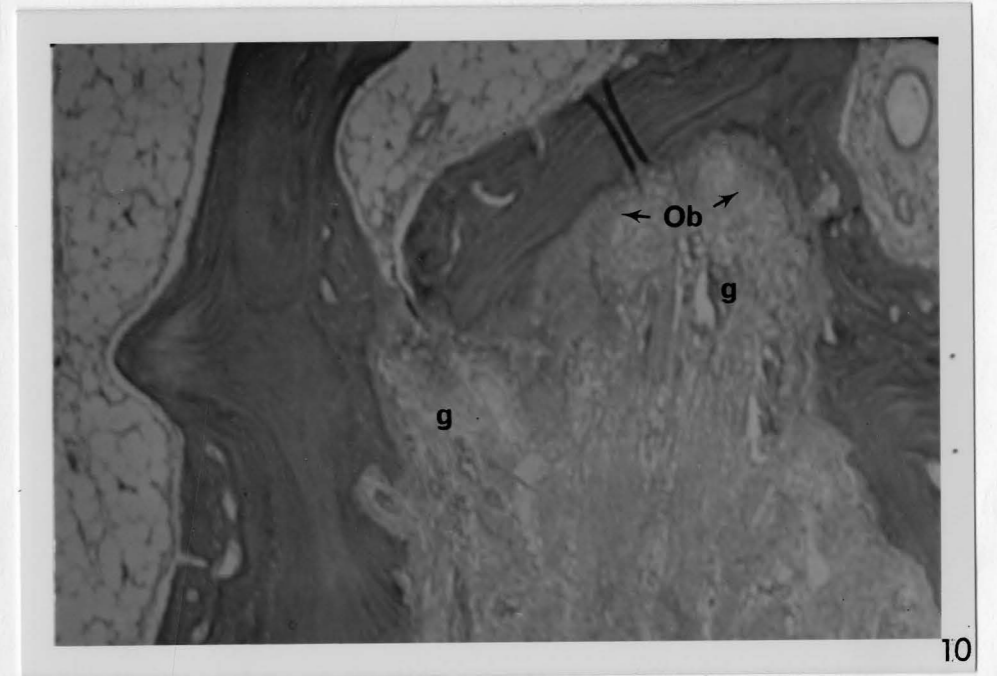


Fig. 11 Thirty day specimen irrigated with saline; Osteoclasts (Oc) adjacent to resorbing bone (ab); Chronic inflammatory cells (CIC); root apex (A); Hematoxylin and eosin stain; X40.

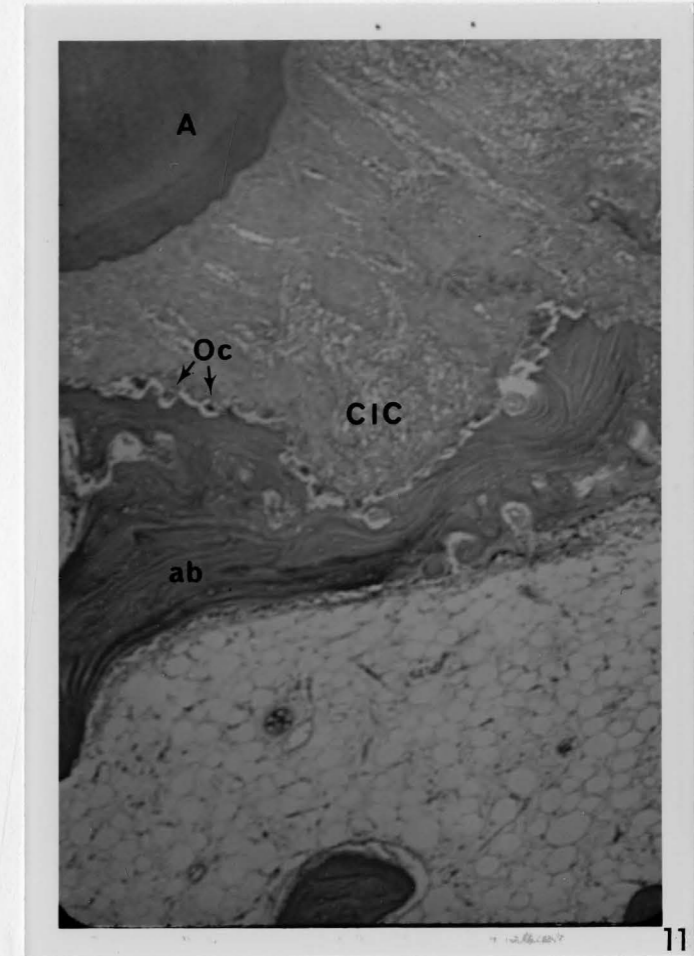
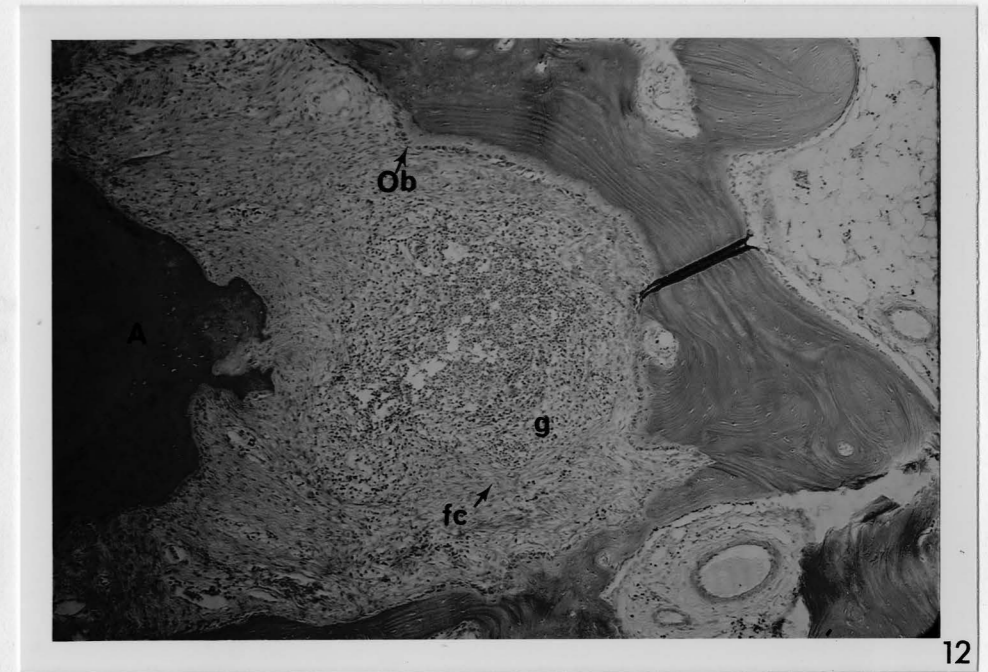
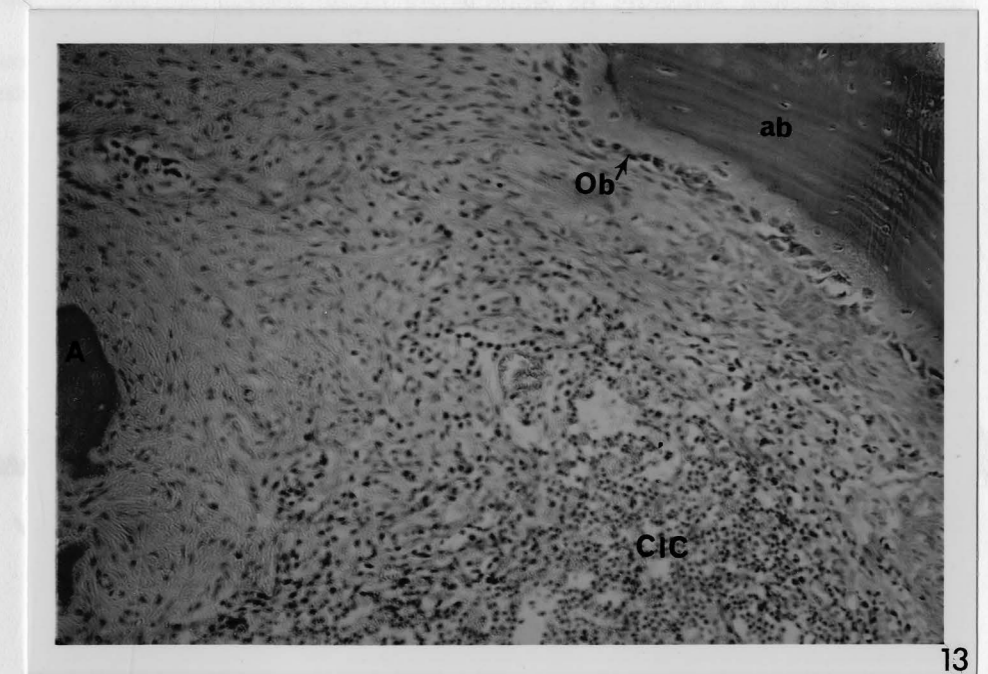


Fig. 12 Thirty day specimen irrigated with saline; Granulation tissue (g) surrounded by fibrous capsule (fc); Osteoblastic (Ob) activity seen adjacent to lesion; root apex (A); Hematoxylin and eosin stain; X40.



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Fig. 13 Thirty day specimen irrigated with saline; Fig. 12 lower center X100 power showing osteoblasts (Ob) forming new bone (ab); Chronic inflammatory cells (CIC); root apex (A); Hematoxylin and eosin stain; X100.



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APPROVAL SHEET

The thesis submitted by John William Gillan 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.

Hal D. McReynolds, Ph.D.

May 22, 1978  
Date

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Signature of Director