PULPAL RESPONSES TO VARIATIONS IN THE FORMOCRESOL
PULPOTOMY TECHNIQUE: A HISTOLOGICAL STUDY

A Thesis

Presented in Partial Fulfillment of the Requirements
for the Degree Master of Science

by

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Introduction

For many years a formocresol pulpotomy has been used in treating exposed dental pulps of primary teeth. The rationale behind the formula and application procedures was not clear and in reading the literature, I found that these procedures had evolved through clinical trial rather than through scientific investigation. The concentration of the drug, the application time, and the composition of the dressing have been arbitrarily determined. Though recent clinical and histological studies have demonstrated the effectiveness of the drug and described the pulpal response, little study has been made of how each of these elements affect the pulpal response.

To determine the rationale for the presently accepted procedure, a pilot study was designed to survey the effect of variations of these elements on the pulpal response. The design of the main study was based on the results of the preliminary survey.
Literature Review

Formocresol, a mixture of 35 per cent cresol and 19 per cent formaldehyde in an aqueous glycerin solution, was recommended as a pulpal medication in 1904 by Buckley (1). In 1936 Sweet (2) presented a technique for its use on exposed pulps in primary teeth. Subsequent descriptions of techniques were made during the next twenty years by Sweet (3, 4) Sweet and Beechan (5), and Sweet, Jr. (6, 7). None of these articles were supported by scientific evidence regarding clinical or histological effect. The use of formocresol has been condemned by one author (8).

Recently, however, scientific investigations have been reported. Controlled studies by Doyle, McDonald, and Mitchell (9) and Spedding, Mitchell, and McDonald (10) and clinical studies by Law and Lewis (11), Shoemaker (12), Via (13), Law (14), and Sweet, Jr. (15) have indicated that formocresol is more successful in treating primary teeth following a pulpotomy than calcium hydroxide, the previous standard medication following pulpotomies.

Investigators have reported histological studies that indicate formocresol is a safe, effective medication (9, 10, 16, 17, 18, 19, 20). These investigators generally agree that the action of formocresol is a non-physiologic fixation, an in vivo precipitation of the proteins in the ground substance. They disagree on the amount of tissue so affected.

Massler and Mansukhani (16) studied the action of formocresol on
rat and human teeth. They reported that the surface of amputated human pulp following a pulpotomy became fibrous and acidophilic within a few minutes after the drug was applied. After seven days of contact with the drug the pulp tissue showed three zones: a broad acidophilic zone (fixation); a broad pale-staining zone (atrophy); and a broad zone of inflammatory cells blending into the remaining normal pulp tissue. With continued contact a progressive fixation of the pulp tissue occurred, with ultimate fibrosis of the entire pulp within 60 days. The rat pulp demonstrated a defensive and reparative response not seen in the human pulp. A heavy band of connective tissue formed between the inflammatory reaction at the amputation site and the normal pulp below. Ultimately a dentin bridge formed by calcification of the connective tissue band.

After sealing formocresol over the amputated pulp stumps of rat and human teeth for periods of five minutes to 28 days, Emmerson and co-workers (17) removed the drug and restored the teeth. The teeth were extracted two to eight weeks later. The pulp reaction varied from surface fixation to complete calcific degeneration, depending on the length of drug application. In short-period applications normal pulp tissue remained below the fixed tissue. Inflammatory cells were absent in all specimens.

Dietz (18) described the histologic effects of formocresol on the non-curious human primary cuspids. A cotton pledget with formocresol was sealed over the pulp stumps. After seven days the pulp stumps were wiped with formocresol and a zinc oxide-eugenol cement was placed in the entire chamber and cavity preparation. The teeth
were removed at intervals ranging from 24 hours to 16 weeks. In the early specimens Dietz noted that the pulpal tissue formed a collagenous-like band which seemed to wall off the surface necrosis produced by the medicament. Later specimens demonstrated a progressive organization of this band with proliferating young fibroblasts infiltrating into it and into the underlying tissue, especially along the periphery of the pulp canals. The development of the band and the cellular activity observed in the area over the 16-week period prompted Dietz to conclude that this zone contained vital tissue. In the 16-week specimens the entire pulpal tissue was undergoing degenerative changes. New tissue composed of fibroblasts which were infiltrating through the apex appeared to be replacing the degenerating tissue. The greatest tissue breakdown was found in the middle portion of the root canal and the least in the apical region. Calcification within the tissue and mild inflammation were seen in a few specimens. No secondary dentin formation was found at any time.

Doyle and co-workers (9) reported a histologic picture in human primary teeth similar to that in the seven-day specimens described by Massler et al (16), except that no calcification or inflammatory process was observed. Pulpotomies were performed on non-carious teeth and the drug was in contact with the pulp for up to seven days.

Spedding and co-workers' (10) results agreed with Doyle's. Studying the primary teeth of rhesus monkeys, he found more unaffected pulp remaining in the apical portion of the root canal. A one-appointment five-minute formocresol application technique was used.
Burgor (19) studied the primary molars of children and followed the same application technique as Speeding. He observed compressed tissue in the coronal portion of the pulp canal blending into an area completely lacking in cellular detail in the apical third. In the seven-week specimens there was an in-growth of granulation tissue through the apical foramen which replaced the tissue in the canals. This granulation tissue appeared progressively more coronal in later specimens. At 35 to 38 weeks it was in close proximity to or in contact with the amputation site.

Beaver, Kopel, and Sabes (20) studied the effects of formocresol in the operative dressing following a formocresol pulpotomy. The pulpotomies were performed on primary molars that were cariously exposed, or nearly so. Following a five-minute application of the formocresol, half of the teeth were covered with plain zinc oxide-eugenol and the rest with zinc oxide-eugenol and formocresol. All were restored with amalgam. The teeth were extracted one, two, and three months after the pulpotomy procedure. The findings resembled those of Dietz. These investigators, however, did not observe the formation of collagenous-like bands of tissue. An ingrowth of fibroblasts through the apex was not observed. Rather, the proliferating fibroblasts represented a metaplastic process induced by the original application of formocresol which resulted in fibrotic tissue.

The use of formocresol as a medication in pulpotomy procedures is described and advocated in standard textbooks on children's dentistry (21, 22, 23). These authors generally describe a two-stage medication
technique similar to that used by Doyle. However, Spedding (24) reported a recent survey of dental schools which indicated that most schools are teaching a one-appointment, five-minute formocresol application technique similar to that used by Spedding et al (10) and Burger (18).

To my knowledge no reports have yet compared the clinical effectiveness of the one-appointment and two-appointment application techniques, nor has the histological effect of application times of less than five minutes been reported.
Preliminary Study

This study was a survey of the effect that variations in the concentration and application time of formocresol, and the type of operative dressing produced on the pulpal response following a pulpotomy. The purpose of this preliminary survey was to establish a means for selecting variables for further study.

Method and Materials

The pulpotomies were performed on the primary cuspids and molars of a female rhesus monkey (M. Mulatta) between three and four years of age. This animal was used because of the experimental nature of the investigation and the dental similarities between this species and man.

The monkey was first tranquillized with serpyn, removed from the cage, scrubbed and clipped, and placed on the table in the operating room. Atropine was administered to reduce salivary flow and counteract vagal stimulation from the anesthetic. Fluothane, nitrous oxide, and oxygen was administered with a face mask. When sufficiently relaxed, the monkey was orally intubated and the desired plane of anesthesia obtained. During this period the monkey was draped with towels and secured in position on the table with tape and small sand bags. The head was allowed to tip back by propping the neck with a towel rolled into a cylinder. A throat pack was placed and the monkey's eyes protected with boric acid ointment. Just before each quadrant was operated, the teeth were wiped with a 2" x 2" gauze sponge moistened
with 70 percent alcohol. The area was dried and isolated with similar gauze pads.

The tooth were opened and the gross tooth structure removed with sterile #2 and #1/2 carbide round burs and a high speed handpiece. The molars were prepared from the occlusal surface and the cuspid from the lingual surface. A conventional speed dental engine and handpiece and sterile #2 and #1/2 round burs were used to open into the pulp chamber and remove the coronal pulp. A bulb syringe was used to blow out dentin chips before switching to the slow speed. Small spoon excavators were also used to aid in removal of the coronal pulp, and to clean debris from the chamber. Small pellets of cotton moistened with distilled water were used to control hemorrhage and finish cleaning the chamber.

Following the surgical technique on each tooth, formocresol was applied to the pulpal stumps in different concentrations and for different application periods. To accomplish this, a cotton pellet was moistened with the drug, blotted on a gauze sponge, and placed in the chamber. A dry cotton pellet was used to gently press the drug-saturated pellet against the pulp stump. The half and quarter strength solutions were prepared by diluting the commercial solution with aqueous glycerin. The application period was timed with a stop watch and a Kodak timer and terminated by removing the cotton pellet and cleansing the pulp chamber with cotton pellets and distilled water. Following the drug application the pulp chamber was filled with either zinc oxide eugenol or zinc oxide eugenol with formocresol. The covering material was mixed to a semi-paste consistency. Equal parts of
eugenol and formocresol were used to mix the dressing containing formocresol. Both types of dressing contained three per cent zinc acetate crystals to accelerate the setting. The paste was placed in the chamber and gently tamped into place with a dry cotton pellet. After the dressing had set, the excess was removed and the area cleaned with gauze sponges and distilled water.

The same procedure was followed in the remaining three quadrants.

The medication and treatment schedule for the 12 teeth was as follows:

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Application Time</th>
<th>Concentration of Formocresol</th>
<th>Covering Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>E</td>
<td>1</td>
<td>15 seconds</td>
<td>Full strength</td>
</tr>
<tr>
<td>D</td>
<td>2</td>
<td>15 seconds</td>
<td>Half Strength</td>
</tr>
<tr>
<td>C</td>
<td>3</td>
<td>15 seconds</td>
<td>Quarter strength</td>
</tr>
<tr>
<td>C</td>
<td>4</td>
<td>15 seconds</td>
<td>Full strength</td>
</tr>
<tr>
<td>D</td>
<td>5</td>
<td>15 seconds</td>
<td>Half strength</td>
</tr>
<tr>
<td>E</td>
<td>6</td>
<td>15 seconds</td>
<td>Quarter strength</td>
</tr>
<tr>
<td>E</td>
<td>7</td>
<td>5 minutes</td>
<td>Full strength</td>
</tr>
<tr>
<td>D</td>
<td>8</td>
<td>5 minutes</td>
<td>Half strength</td>
</tr>
<tr>
<td>C</td>
<td>9</td>
<td>5 minutes</td>
<td>Full strength</td>
</tr>
<tr>
<td>C</td>
<td>10</td>
<td>5 minutes</td>
<td>Half strength</td>
</tr>
<tr>
<td>D</td>
<td>11</td>
<td>5 minutes</td>
<td>Quarter strength</td>
</tr>
<tr>
<td>E</td>
<td>12</td>
<td>No application</td>
<td></td>
</tr>
</tbody>
</table>

Upon completion of the procedure the endotrachael tube was removed and the monkey placed in a baby incubator. After recovering from the anesthesia, the monkey was returned to the cage.

After three weeks the monkey was again anesthetized with the previously described procedure. The 12 primary teeth were removed with a small half-round elevator and dental forceps.

To facilitate fixation, dentin and cementum were removed from the mesial and distal root surfaces of each specimen with a carborundum stone, under water, until a faint outline of the pulp was visible.
The specimens were placed in 10 per cent formalin solution for four days and decalcified in trichloracetic acid for two weeks. After 24 hours in water, they were dehydrated in alcohol and dioxane, infiltrated with melted paraffin for four days, and imbedded in paraffin. Six micron serial sections were cut and stained with hematoxylin and eosin.

Results

In order to test as many combinations as possible of the three procedure variables, concentration of drug, length of application and type of covering, all the available teeth were treated. No untreated pulps were left as controls. Therefore, the results took the form of a qualitative comparison rather than a descriptive interpretation of the pulpal response. Following the main study, normal pulp was available and the histological responses of these teeth were described.

The histologic specimens were coded to prevent bias during microscopic evaluation. No dramatic differences were noted in the specimens and all were considered successful pulpotomies. Variations in the technique did not produce remarkably different histologic results. Enough difference existed, however, to group the slides into two general categories. Those specimens presenting normal appearing pulp tissue in the major portion of the canal, with the affected tissue confined to the coronal one-third of the canal, were considered to demonstrate a mild response. When the tissue response extended into the middle one-third of the canal the response was considered severe.
When decoded, it was found that the five-minute application produced the more severe response and the 15-second application the milder response. Variations in the concentration of the solution apparently had no effect. No definite conclusions could be drawn concerning the inclusion of formocresol in the dressing. Specimen No. 2 was lost during histologic preparation.

Table of Results

<table>
<thead>
<tr>
<th>Specimen No.</th>
<th>Application Time</th>
<th>Concentration of formocresol</th>
<th>Covering Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
<td>15 seconds</td>
<td>Full strength</td>
<td>ZOE</td>
</tr>
<tr>
<td>3</td>
<td>15 seconds</td>
<td>Quarter strength</td>
<td>ZOE - FMC</td>
</tr>
<tr>
<td>5</td>
<td>15 seconds</td>
<td>Half strength</td>
<td>ZOE</td>
</tr>
<tr>
<td>6</td>
<td>15 seconds</td>
<td>Half strength</td>
<td>ZOE - FMC</td>
</tr>
<tr>
<td>1</td>
<td>15 seconds</td>
<td>Quarter strength</td>
<td>ZOE</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Specimen No.</th>
<th>Application Time</th>
<th>Concentration of formocresol</th>
<th>Covering Material</th>
</tr>
</thead>
<tbody>
<tr>
<td>8</td>
<td>5 minutes</td>
<td>Half strength</td>
<td>ZOE - FMC</td>
</tr>
<tr>
<td>7</td>
<td>5 minutes</td>
<td>Full strength</td>
<td>ZOE - FMC</td>
</tr>
<tr>
<td>12</td>
<td>No application</td>
<td></td>
<td>ZOE - FMC</td>
</tr>
<tr>
<td>11</td>
<td>5 minutes</td>
<td>Quarter strength</td>
<td>ZOE</td>
</tr>
<tr>
<td>10</td>
<td>5 minutes</td>
<td>Half strength</td>
<td>ZOE</td>
</tr>
<tr>
<td>9</td>
<td>5 minutes</td>
<td>Full strength</td>
<td>ZOE</td>
</tr>
</tbody>
</table>
Experimental Procedure

The primary teeth of a male and a female monkey (M. Mulatta), both 13 months old and healthy, were treated in this study. The primary cuspsids and molars were divided into four groups. Each group contained an upper buccal quadrant of teeth from one monkey and the opposite lower buccal quadrant from the other. Each group, therefore, contained six teeth and each monkey contributed three teeth to each group.

The monkeys were prepared and the surgical procedure conducted on the teeth in Groups I, II, and III in the manner described in the pilot study. Teeth in Group IV were not operated. The teeth in Group I received a five-minute application of full strength formocresol and those in Group II a 15-second application. The drug was applied, timed, and withdrawn using the same procedure described in the pilot study. The teeth in Group III received no application of formocresol. The pulpal stumps in all three groups were covered with a dressing of zinc oxide-eugenol containing formocresol. This covering was mixed as described in the pilot study.

Four weeks after the pulpotomy procedure the teeth were removed using a half round elevator and pedodontic forceps. The occlusal and apical areas were opened with a round bur and a conventional hand piece to aid the pulpal fixation and all the teeth were placed in 10 per cent formalin. The histological preparation was carried out as described in the pilot study, except that the root structure was
not removed from the root surfaces. Seven-micron serial sections were prepared for evaluation.
Results

The pulpal tissue of Group I (five-minute application of formocresol) appeared to be undergoing a fibrous metaplasia. This change was seen in the upper two-thirds of the pulpal canal of all specimens. The response varied from moderate to complete fibrosis at this site. An inflammatory response was not seen. In the more fibrous pulps there was a tendency toward calcification (Figures 1 - 3). The fibrous tissue immediately adjacent to the amputation site tended to be organized into a band or sling. An additive type of osteodentin was seen at the dentinal wall of three canals (Figures 4 - 5). Normal pulpal tissue was consistently observed in the apical portions of the canals.

The pulpal tissue in one specimen appeared to be in an earlier stage of the response than the other teeth (Figures 6 - 7). A dark staining compressed fibrous band was present at the amputation site. The few cells present above the band appeared enlarged and dark staining. The tissue immediately below the band was very loose and reticular, and showed a tendency toward vacuolation. The odontoblasts appeared normal. Apical to this area, an inflammatory reaction was present. Osteodentin was observed in the middle and lower portions of the canal.

The fibrous change was present in all specimens in Group II (15 second application of formocresol. The degree of fibrosis varied. No calcification or inflammatory response was observed. All but two specimens exhibited band formation of the fibrous tissue at the amputation site. One was so well organized that it resembled a periodontal
ligament (Figures 8 - 11). Osteodentin formation was prominent in two specimens. Normal pulp was present in the apical third of all specimens. Mild hyperemia was present in two specimens.

In Group III (no application of formocresol) the crown of one specimen had been fractured prior to extraction and most of the pulpal covering was lost. The pulp was completely necrotic.

The pulpal response in the remaining five specimens was a fibrous metaplasia. The degree of fibrous change again varied. An inflammatory response was not seen. Three of the five exhibited band formation of the fibrous tissue (Figures 12 - 14). One specimen exhibited complete fibrous metaplasia from the amputation site to the apex, as well as marked pulpal calcification (Figures 15 - 19). Osteodentin was prominent in one specimen. Hyperemia was present in one specimen. The specimens contained normal tissue in the apical third of the canal.

After the main study was completed, the histological response of the teeth in the preliminary study was evaluated.

The pulpal response in these teeth was a fibrous metaplasia. One specimen exhibited fibrous tissue from the amputation site to the apical third of the canal (Figures 20 - 22). However, the vertical strands of fibrous tissue and vascularity seen in the apical third of this specimen did not differ in appearance from apical tissue in some of the untreated monkey pulps from the main study. In most of the specimens the fibrous change was definitely limited to the coronal third of the canal. Fibroblasts in this area appeared young and in an early stage of organization (Figures 23 - 25). A tendency for band formation was
apparent, but no specimen exhibited a well developed band (Figures 26 - 28). Secondary dentin formation was present along the walls of the canals near the amputation site. Apical to the fibrous response normal pulpal tissue was observed. Increased vascularity was often seen in the middle and lower portions of the canal.

When divided into groups according to application time, concentration of the drug, or type of covering, no difference in the pulpal response could be detected. Therefore, the earlier impression that the teeth could be divided into a mild and a severe group was not valid.
Discussion

The purpose of this investigation was to determine whether certain variations in the formocresol pulpotomy procedure would affect the pulpal response.

Until the late 1950s this technique was thought to produce pulp mummification and was considered a non-vital technique. Massler and Mansukhani (16) in 1959 reported histological findings described as "fixed tissue." They suggested that "fixation" of the living tissue was produced by the formaldehyde which precipitated the proteins in the ground substance, in vivo. There has been disagreement, however, as to whether this phenomenon, described as fixed tissue, is a normal physiologic response and, therefore, whether the procedure itself should be classified as vital or non-vital.

The pulpal response observed in this study was a fibrous metaplasia, indicative of a normal reparative response, with a tendency for the fibrous tissue to organize into a sling-like band. The fibrous change was not equally developed in all specimens or in all areas of individual specimens. Some specimens appeared to be generally in an earlier stage, while a more advanced fibrous response was seen in others. When the sling-like fibrous organization was observed, it was near the amputation site.

In the specimens showing generally an early stage of fibrous change, a dark staining compressed fibrous band was seen at the amputation site with large dark staining cells superficial to the band.
Previous investigators have observed a similar pulpal response to formocresol at the amputation site. Massler and Mansukhani (16) reported that the pulp immediately under the formocresol became fibrous and eosinophilic. They suggested that this was a layer of fixed tissue, wherein the protein in the ground substance was precipitated by the formaldehyde in vivo. This fixed tissue did not appear as normal healthy pulp. Rather it was described as being sharply demarcated from the underlying normal pulp.

Spedding et al (10) and Doyle et al (9) also described a fibrous and eosinophilic fixed zone immediately beneath the medicament. Dietz (18) described a zone at the amputation site, corresponding to the fixed zone described by Massler et al (16), containing cells and a collagenous-like intercellular substance which appeared fibrous and seemed to wall off the surface necrosis. Dietz observed cellular changes in this area, however, and considered this zone to be vital.

Emmerson et al (17) reported a homogeneous yellow staining band at the amputation site. Below, the pulp appeared normal. This area of normal-appearing tissue was present regardless of the application time and was considered to be fixed in vivo because pulpal degeneration was observed below this zone. Burger (19) described the pulpal tissue at the amputation site as well defined and compressed. He also considered the tissue fixed because of the well outlined cellular detail and necrotic changes apical to this zone.

Beaver et al (20) described a variety of reactions in the coronal pulp, but no characteristic response of the tissue was seen immediately adjacent to the amputation site.
The response seen in the present study at the amputation site in the early stage appeared similar to that described by previous investigators. The response particularly resembled the findings of Dietz (18). The formocresol produced what appeared to be a precipitation of the protein in vivo; however, this occurred only in cells immediately adjacent to the drug. This phenomenon was considered to be the same as the "fixation" described by others. These cells and their nuclei were enlarged and stained very dark. This fixation reaction appeared to affect central tissue more than peripheral tissue. Occasionally a cluster of these cells appeared isolated in the coronal pulp. These areas might be continuous with those seen at the amputation site, and the apparent isolation might be explained by the angle of sectioning. Bordering these fixed cells near the amputation site was a layer of cells which appeared as a compressed fibrous band. The fibrous change appeared to begin in the tissue adjacent to the band. The most advanced fibrotic reaction was observed in the coronal portion of the canal in specimens generally showing a more advanced response, and areas of earlier fibrous change were observed to progress apically. The young developing fibroblasts and blood vessels in the more apical areas of very early change gave the appearance of granulation tissue. Near the amputation site the developing fibroblasts tended to organize into a sling-like band.

In all specimens normal-appearing tissue, when observed, was found in the most apical portion of the canal. An overview of these findings suggests an orderly repair reaction of the tissue with the
fartherest advancement of the fibrous change nearest the amputation site. The development of this fibrous tissue strongly suggests that the response to this technique may be considered a vital one.

When the response was well developed the dark staining cells and compressed band were not seen or remained only in small clusters. In the second-week specimens Dietz (18) described a new pulpal network of young proliferating fibroblasts immediately below the collagenous band and infiltrating into it. Perhaps this phenomenon accounts for the organization of the fibrous tissue and loss of the compressed appearance. The pulp may have removed these fixed cells or they may have degenerated and contributed to the debris often seen above the amputation site. It is also possible that the cells comprising the early band develop into mature fibrous tissue.

The ingrowth of new tissue composed of fibroblasts which infiltrated through the apex and replaced degenerative pulpal tissue which was described by Dietz (18) and Burger (19) was not observed. However, the areas of early fibrous change described in the present study gave the appearance of granulation tissue. The difference between these findings and those describing an ingrowth may be the result of a different chronological interpretation of the same response.

Beaver and co-workers (20) also failed to find evidence of an ingrowing fibrotic and granulation tissue. Moreover, their general conclusions were similar to those of this study. They believed that there had been a metaplastic process induced by the original application of formocresol which stimulated the formation of fibrotic tissue.
They believed that this response resembles an aging process and suggested that formocresol may be enough of an irritant to speed up the aging process of the pulpal tissue without producing degeneration and necrosis.

Secondary or osteodentin and pulpal calcifications were observed in some specimens. Profound secondary dentin occurred along the walls of the coronal third of the canal, always in association with the fibrous change. Often cells could be seen trapped within the calcified material. Similar findings were reported by Emmerson et al (17), Spedding et al (10), and Beaver et al (20). Such calcifications might also be considered part of the aging process and indicative of a vital pulp. There were no odontoblasts adjacent to those areas of profound secondary dentin formation, but these cells were observed in a typical relationship to the dentin walls in areas of normal-appearing tissue. The impression from these findings is that there was accelerated activity of the odontoblasts, producing this reparative dentin so rapidly that some of the cells were trapped. Then as the metaplastic process began, activity ceased and the odontoblasts were replaced by the fibroblasts.

Massler et al (16), Burger (19), and Beaver et al (20) reported inflammation as a typical finding. Beaver and co-workers (20) considered it a sign of a potential metaplastic or healing response. In this study evidence of an inflammatory response was not observed frequently enough to consider it a typical finding. It is likely, however, that an inflammatory response preceded the metaplastic change and disappeared before the teeth were removed.
Necrosis in the middle third of the pulp chamber was reported by Emmerson et al. (17), Dietz (18), Doyle et al. (9), and Burger (19). In this study what appeared to be post-extraction autolysis was observed in only a few specimens and only in those with narrow canals. The greatest breakdown of the tissue occurred in the middle third of the canal, the area requiring the greatest penetration of the histologic fixative. This could be mistaken for pre-extraction necrosis. A lack of tissue reaction in the area of the dying or dead cells in this investigation suggested that this response was post-extraction autolysis. In the main study dentin was not removed from the root surfaces as part of the histologic preparation. Adequate fixation as seen in the preliminary study was probably due to the removal of some root structure. Therefore, it is suggested that in future studies root structure be removed from specimens, especially if a narrow canal is suspected. This would aid in fixation and avoid the confusion in interpretation created by areas of post-extraction autolysis.

Histologic studies published in 1959 by Massler et al. (16) and Emmerson et al. (17) suggested that the extent of pulpal fixation might be reduced by decreasing the drug application time, resulting in a vital technique.

Massler and Mansukhani (16) found that the pulp immediately under the amputation site became fibrous and acidophilic shortly after drug application. Continued application produced progressive fixation of the remaining pulpal tissue. The fixed zone seen shortly after drug application extended much deeper into the pulp canal when the drug was
applied under pressure. The zone was much narrower or even absent when
dentin chips and debris intervened between the drug and the pulpal
tissue, or when the drug was mixed with zinc oxide-eugenol instead of
being applied on a cotton pellet. They suggested that the formocresol
be removed after two to three days to prevent the progressive fixation
(mummification) of the entire pulp.

Emmerson et al (17) reported that changes in the pulpal tissue
varied from surface fixation to complete calcific degeneration depending
on the total time that formocresol was in contact with the amputated
pulp.

Dietz (18) and Doyle et al (9), using a two-appointment procedure,
found vital tissue in the apical portions of the canals. However,
Doyle and co-workers (9) reported that the principal effects of formo-
cresol on the primary dental pulp occurred in four days or less.
Spedding et al (10), Burger (19), and Beaver et al (20), using a one-
appointment procedure, described relatively more vital tissue present.
All these findings suggest that reducing the drug application results
in more vital tissue remaining in the pulp canal. The shortest appli-
cation period reported is five minutes, with the drug not being included
in the operative dressing.

In comparing the three application of the drug no difference in
the pulpal response could be detected. There did appear to be a slight
difference in the responses of the two monkeys. The specimens from
one tended to show a more advanced response. Specimens from the pre-
liminary study were in an earlier stage of the response. Since the
specimens from the preliminary study were removed a week earlier than the
other specimens, a less developed pulpal response was predictable. Also the monkey used in the preliminary study was three to four years old and the two used in the main study were 13 months old. These findings indicate that individual differences, such as age, state of health, and constitutional factors, may affect the rate of progress of the pulpal response. To better determine the typical response for a given group, more specimens are needed.

Variations were also observed in the pulpal response between specimens within each group. Operating on nine teeth at one appointment under general anesthesia may have produced enough systemic stress to alter the vascular and other defense mechanisms and thus contribute to the variations observed between specimens. Dentin chips and debris were hard to remove and may have been the greatest contributor to the variations observed. Massler et al (16) indicated that dentin chips might serve as a barrier reducing the affect of the drug. Perhaps a high-volume suction would have more effectively debrided the pulp chambers and allowed for more consistent response.

Since no untoward effect upon the pulpal response of the monkey was detected that could be attributed to the length of application time, a study of the effect of the shorter application times on human pulp might be warranted. Previous histological studies (9, 10, 16, 17, 18, 19, 20) suggest that human pulp may be more sensitive to variations in procedure, and an application time less than those currently suggested might reduce the insult to the pulp and produce the vital, fibrotic response observed in this study. A comparison of the varying histological results reported in studies of human teeth by various
authors, and in some cases by the same author using different application procedures, tend to support this hypothesis. Less desirable results apparently occur when application times are prolonged.

Another step in the formocresol procedure open to question as a result of this and other studies involves the addition of formocresol to the pulp dressing. Massler et al (16) reported a reduction in the amount of fixed tissue when the formocresol was mixed with the zinc oxide-eugenol, instead of being applied on a cotton pellet. In the present study no difference could be detected between the group which received formocresol on a cotton pellet and then a formocresol and zinc oxide-eugenol dressing and the group which received only the formocresol and zinc oxide-eugenol dressing. On the other hand, Beaver and co-workers (20) reported no difference in the pulpal response, whether formocresol was included in the operative dressing or not, following direct application of the formocresol on a cotton pellet.

In the preliminary study no difference could be detected between the specimens with or without formocresol in the operative dressing. Since both application techniques alone - that is, direct application or inclusion in the operative dressing - produce comparable results, one or the other would seem sufficient and the use of both unnecessary.
Summary and Conclusions

Formocresol pulpotomies were performed on the primary cuspids and molars of three rhesus monkeys. The first monkey was used to survey variations in the technique to determine the design of the main study.

The main study included two monkeys. The 24 primary cuspids and molars were divided into four groups. Pulpotomies were performed on the teeth in Groups I, II, and III. The teeth in Group IV served as a control. The teeth in Group I received a five-minute application of formocresol, and those in Group II a 15 second application. The teeth in Group III received no application of formocresol. The pulpal stumps in all three groups were covered with a dressing of zinc oxide-eugenol containing formocresol. All the teeth were extracted four weeks later.

Histologically, the pulpal response to formocresol was a fibrous metaplasia. The fibrous tissue tended to become organized into a sling-like band near the amputation site forming what appeared to be a barrier.

No differences in the pulpal response of the three groups could be detected. Comparable results were obtained by applying the drug directly or by mixing the drug in the operative dressing. Therefore, one method or the other would seem sufficient and the use of both unnecessary.

An overview of these findings suggests an orderly repair reaction of the tissue and indicates that the response may be considered a vital one.
Since no undesirable effect on the pulpal response of the monkey was detected in this study, a study of the effect of the application times of less than five minutes on human pulp is warranted. Previous histological studies suggest that human pulp is more sensitive to variations in procedure, and application times less than those currently suggested might reduce the insult to the pulp and produce the vital, fibrotic response observed in this study.
Illustrations
Figure 1. (35X) Mandibular left second molar treated for five minutes with formocresol and covered for four weeks with zinc oxide-eugenol containing formocresol. The amputation site and coronal third of the pulp canal are seen. The pulp shows a general fibrous response with a tendency toward band formation. A large area of calcification is seen in the center of the coronal pulp with two smaller ones below.
Figure 2. (100X) Amputation site of Figure 1 demonstrating the organization of the fibrous tissue and early pulpal calcification in the lower right of the figure.
Figure 3. (100X) Middle portion of the pulp canal in Figure 1 showing the pulpal calcifications, osteodentin along the wall, and the lack of odontoblasts.
Figure 4. (60X) Mandibular left cuspid treated for five minutes with formocresol and covered for four weeks with zinc oxide-eugenol containing formocresol. The coronal half of the pulp canal shows a fibrous response and osteodentin along the dentinal walls.
Figure 5. (270X) The pulp near the amputation site of the specimen in Figure 4 shows organization of fibrous tissue.
Figure 6. (21X) Maxillary right cuspid treated for five minutes with formocresol and covered for four weeks with zinc oxide-eugenol containing formocresol. The coronal half of the canal shows an early response and fixed tissue at the amputation site. Below are a pale zone and an inflammatory zone.
Figure 7. (270X) The junction of the fixed zone and the pale staining zone in Figure 6 is seen showing the appearance of the fixed cells, the compressed deep staining fibrous appearing band and the light staining tissue below.
Figure 8. (60X) Mandibular right cuspid treated for 15 seconds with formocresol and covered for four weeks with zinc oxide-eugenol containing formocresol. Here is seen the ligamentous-like bend organization of the fibrous tissue and the osteodentin along the walls of the canal.
Figure 9. (270X) The junction of the organized fibrous tissue and the osteodentin seen in Figure 8 showing the character of the area and the lack of odontoblasts.
Figure 10. (270X) The area below the fibrous band in Figure 8 showing fibrous tissue and a transition toward less organization.
Figure 11. (270X) The apical area of the specimen in Figure 8 containing normal tissue with odontoblasts.
Figure 12. (60X) The maxillary left primary cuspid received no formocresol directly, and the pulpal stump was covered for four weeks with zinc oxide-eugenol containing formocresol. This specimen shows fibrous tissue in the coronal third of the pulp canal with a tendency for band-like organization, osteodentin along the canal wall, and a lack of odontoblasts.
Figure 13. (270X) Central area of Figure 12 showing fibroblasts and pulpal calcification.
Figure 14. (100X) Middle third of the pulp canal of the specimen in Figure 12 demonstrating a transition from fibrous tissue to normal-appearing pulpal tissue. Odontoblasts appear in the transitional as well as in the normal zone.
Figure 15. (60X) Maxillary left second primary molar received no formocresol directly. The pulpal stump was covered for four weeks with zinc oxide-eugenol containing formocresol. Fixed tissue is present at the amputation site, odontoblasts are not seen, and the fibrous tissue present shows a tendency toward band-like organization.
Figure 16. (35X) The apical half of the specimen in Figure 15 showing fibrous tissue, a lack of odontoblasts, and pulpal calcifications.
Figure 17. (100X) Same specimen as seen in Figure 15, showing fibrous tissue with a tendency toward band formation near the site of amputation.
Figure 18. (270X) Central portion of area seen in Figure 17, showing fibrous character of the tissue.
Figure 19. (100X) Apical third of the pulp canal shown in Figure 16, showing fibrous tissue and pulpal calcifications.
Figure 20. (35X) Maxillary right primary cuspid from the preliminary study treated with quarter strength formocresol for 15 seconds and the pulpal stump covered for three weeks with zinc oxide-eugenol containing formocresol. Fibrous tissue and a lack of odontoblasts are seen.
Figure 21. (100X) Coronal portion of the pulp canal of Figure 20 showing fixed tissue above fibrous tissue.
Figure 22. (100X) Apical third of the pulp canal of the specimen seen in Figure 20, showing fibrous strands and vascularity.
Figure 23. (35X) Mandibular left primary cuspid from the preliminary study was treated with half strength formocresol for five minutes and the pulpal stump was covered for three weeks with plain zinc oxide-eugenol. This shows early fibrous tissue formation near the amputation site.
Figure 24. (100X) Coronal portion of the pulp canal of specimen in Figure 23, showing young fibroblasts in an early stage of organization, dentin chips, and the formation of osteodentin around dying cells and dentin chips.
Figure 25. (100X) Middle of the pulp chamber of specimen in Figure 23 showing normal pulp tissue with odontoblasts, blood vessels and fibrous strands.
Figure 26. (60X). Mandibular left first primary molar from the preliminary study was treated with quarter strength formocresol for five minutes and the pulpal stump was covered with zinc oxide-eugenol. Osteodentin along the walls of the canal near the amputation site, vascularity, and fibrous tissue with a tendency for band organization are shown.
Figure 27. (270X) Pulpal tissue approximating the amputation site in Figure 26, shows the organization of the fibroblasts parallel to the amputation site.
Figure 28. (270X) Pulpal tissue from the coronal portion of the canal of the specimen in Figure 26, shows developing fibrous tissue and vascularity.
References


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