

LEDERMIX™

A Long History as the Leading Clinically Proven Solution.



The Ledermix Materials: Fact or Fiction?

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Endodontist

Introduced by David Redmayne
Ozdent, C.E.O.

The Ledermix Materials – Fact or Fiction?

Scientifically-based Indications for Their Use in Everyday Dentistry

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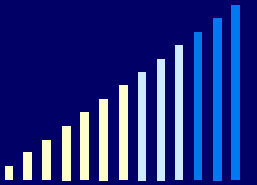
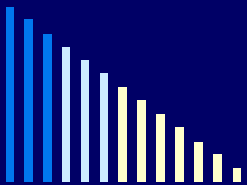


Declaration

Prof. Abbott occasionally acts as a paid Scientific Advisor for OzDent Pty Ltd.

Prof. Abbott is paid by OzDent Pty Ltd to present lectures on occasions.

OzDent do not specify or influence the lecture content at any time or in any manner.



Background Information

◆ Ledermix Paste

- Developed in 1960 (by Prof. André Schroeder)
- Commercially available since 1962
- 59 years of research and clinical use !



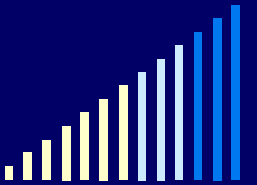
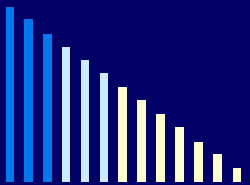
◆ Ledermix Cement

- Developed in 1962



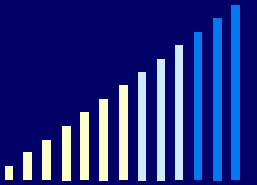
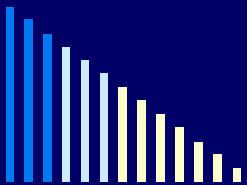
The Ledermix Story

- ◆ Corticosteroids first used in **Endodontics** to treat acute **apical periodontitis** by flushing the canal with hydrocortisone – with “prompt relief of pain” (Wolfsohn 1954)
- ◆ Use of a corticosteroid:antibiotic mixture was reported – “sensitivity to percussion and swelling were reduced dramatically” (Schroeder & Triadan 1961)



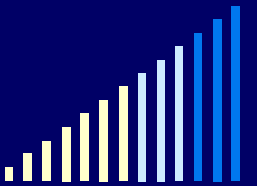
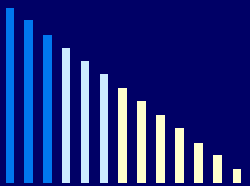
The Ledermix Story

- ◆ Many other clinical reports for treating **apical periodontitis**
 - Schroeder (1962, 1965); Ehrmann (1964, 1965 1972); Olsen (1966); Baume (1968); Schneider (1968); Laws (1969); Erasquin (1972); Barker & Lockett (1971, 1972)
- ◆ And histological reports:
 - Schroeder (1962); Barker & Lockett (1971); Erasquin (1972)



The Ledermix Story

- ◆ Clinical and histological studies done – for pulpitis:
 - Schroeder and Triadan (1961, 1962, 1963, 1968, 1972)
- ◆ Initially used hydrocortisone
- ◆ Then used triamcinolone
 - A more potent CS
- ◆ Combined with: chloramphenicol and xylocaine
 - In an ointment base



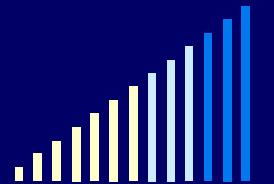
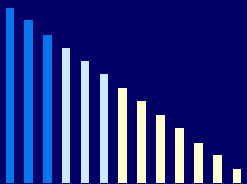
The Ledermix Story

◆ Procedure (Schroeder):

- Remove ALL caries
- Mix the CS:AB paste into a cotton pledget
- Apply to the pulp
- Close the cavity with ZO-E
- One week later - remove the pledget
- Replace with a hard setting capping cement
 - e.g. Ca(OH)_2
- Restore the tooth

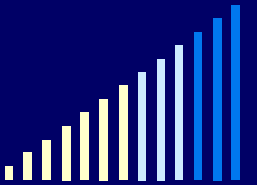
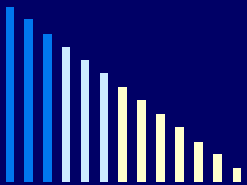


Schroeder 1981



The Ledermix Story

- ◆ Schroeder and Triadan reported outcomes for 200 teeth:
 - Pain disappeared within 2-3 hours
 - Even when suppurative pulpitis
 - Majority of pulps remained healthy
 - Only the suppurative cases needed further treatment (i.e. root canal treatment)



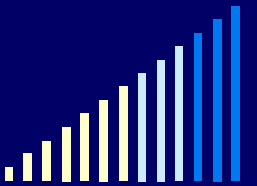
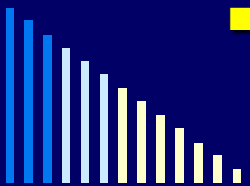
The Ledermix Story

- ◆ Initially: Triamcinolone + Chloramphenicol + Xylocaine
- ◆ In 1962 - Schroeder reported no need to include Xylocaine
- ◆ In 1962 - Ledermix was made commercially
 - BUT - the antibiotic component was changed to Demeclocycline
 - For commercial reasons by (Lederle Pharmaceuticals)



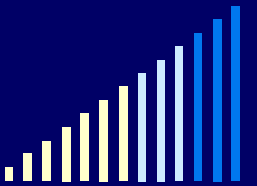
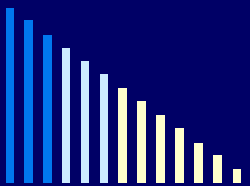
The Ledermix Story

- ◆ Schroeder noted direct pulp capping materials should be:
 - Dentinogenic, anti-bacterial and anti-inflammatory
- ◆ No single material is likely to have all these properties
- ◆ Therefore, he said it is *“appropriate to combine materials”*
- ◆ He used:
 - CS:AB - anti-inflammatory and antibacterial properties
 - Ca(OH)_2 - dentinogenic properties and anti-bacterial
 - ZO-E - anti-inflammatory and anti-bacterial



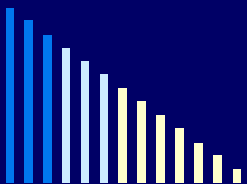
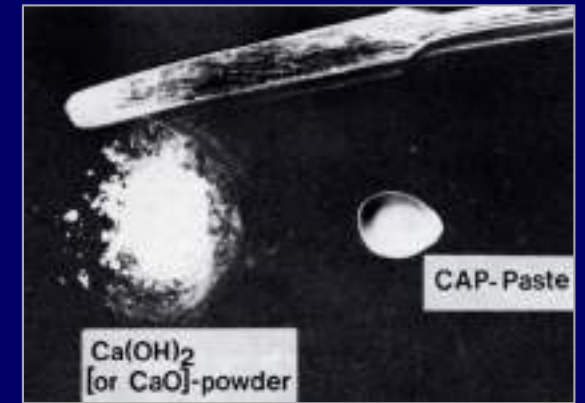
The Ledermix Story

- ◆ Schroeder further stated that the CS has two main goals:
 1. Prevent acute exacerbation of already inflamed tissues
 2. Prevent the necrosis caused by $\text{Ca}(\text{OH})_2$
- ◆ And the ZO-E does not affect the $\text{Ca}(\text{OH})_2$
 - Whereas $\text{Zn}_3(\text{PO}_4)_2$ is acidic and may neutralise the $\text{Ca}(\text{OH})_2$, making it less effective



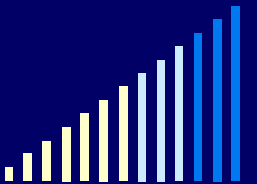
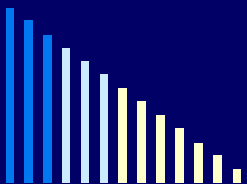
The Ledermix Story

- ◆ So ... Schroeder then mixed equal volumes of Ledermix paste with Ca(OH)_2 powder and applied as a pulp cap
 - After removing ALL caries
 - *The first use of a 50:50 mixture !!!*
- ◆ Then he placed ZO-E
 - As a hard setting base
- ◆ And restored the tooth at the same appointment



The Ledermix Story

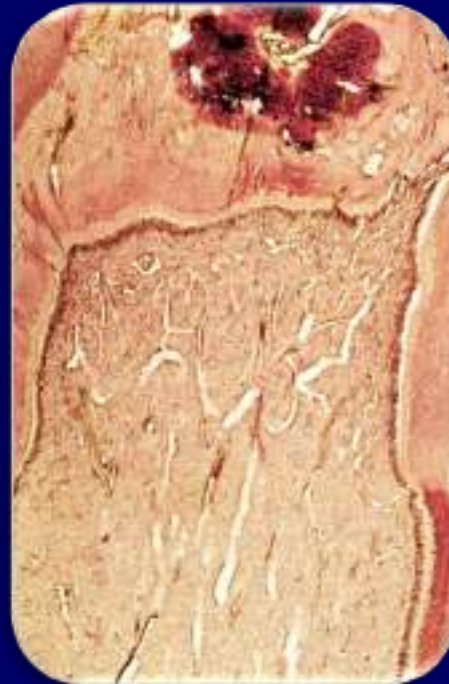
- ◆ So ... Schroeder then mixed equal volumes of Ledermix paste with $\text{Ca}(\text{OH})_2$ powder and applied as a pulp cap
- ◆ *Excellent results were reported !!!*
 - *Rapid pain relief*
 - *Pulps had survived when reviewed*
 - *With pulp tests, radiographs, etc.*



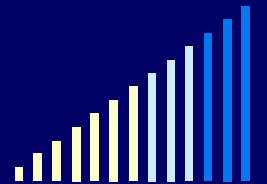
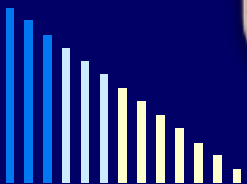
The Ledermix Story

- ◆ Histological evidence of good healing and repair
 - No inflammation in the pulp
 - Some with tertiary dentine formation

In Humans



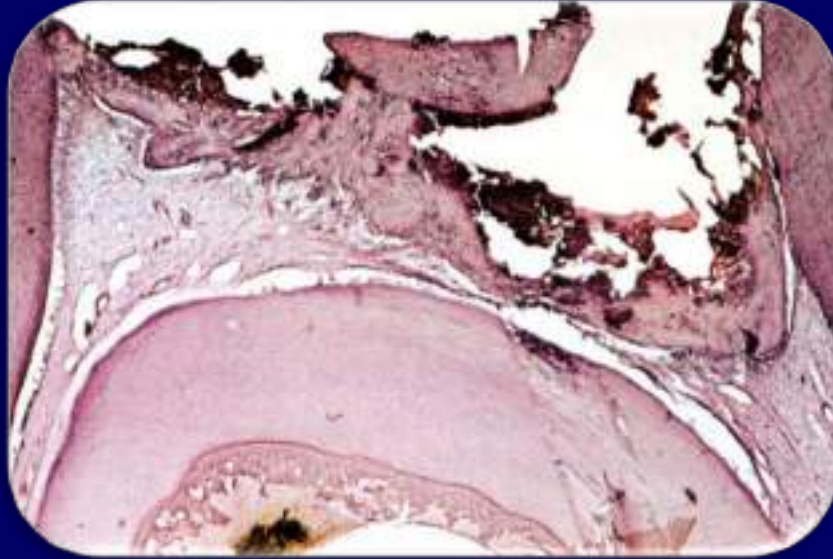
Schroeder
1981



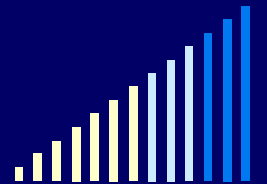
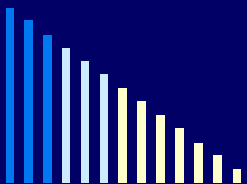
The Ledermix Story

- ◆ Histological evidence of good healing and repair
 - No inflammation in the pulp
 - Some with tertiary dentine formation

In Humans and
in Monkeys

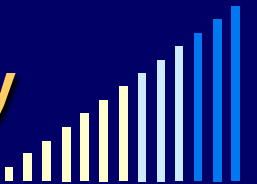
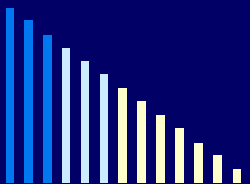


Schroeder
1981



The Ledermix Story

- ◆ Then in 1962, Schroeder developed a hard setting cement
 - Same active substances as the paste
 - ✧ Triamcinolone and Demeclocycline
 - But at lower concentrations - 0.67% and 2%
 - And combined them with ZO-E and Ca(OH)_2
- ◆ The rationale was to:
 - Avoid the need for two appointments
 - Achieve all desired therapeutic aims with one material
 - Have a hard setting compound
 - ease of use
 - can restore immediately



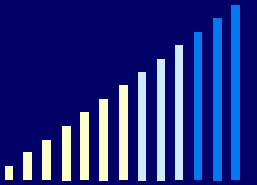
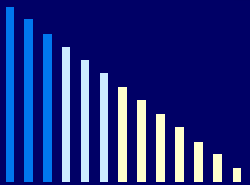
The Ledermix Story

✓ Hence: **Ledermix Cement** was manufactured



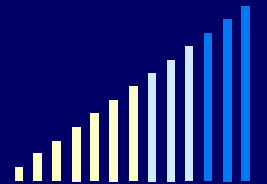
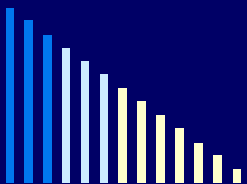
The Ledermix Story

- ◆ BUT - the Ledermix products were controversial
- ◆ Opposition from various people - esp. in the USA
- ◆ Some of the concerns were:
 - Systemic side effects of steroids
 - Inability of steroids to stimulate calcific repair
 - Steroids lead to chronic inflammation and/or pulp necrosis
 - Development of tetracycline-resistant micro-organisms
 - Development of hypersensitivity reactions to tetracyclines
 - More specific anti-microbial agents may be available



The Ledermix Story

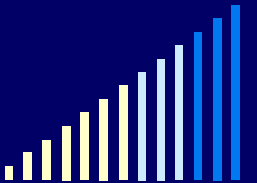
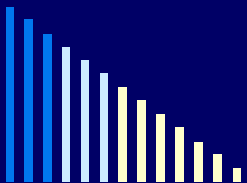
- ◆ Often claimed that Ledermix is “*banned in the USA*”
 - I still **OFTEN** hear this today!!!
- ◆ This is “**FAKE NEWS**” !!!!
 - It has **NEVER** been banned



The Ledermix Story

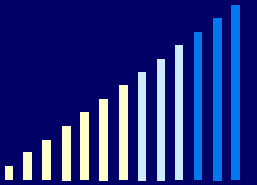
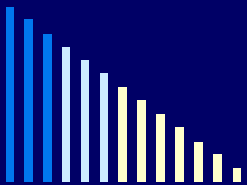
◆ The TRUTH is:

- Lederle Pharmaceuticals have NEVER submitted the Ledermix products to the FDA for approval
- This was a financial decision
 - ➔ In 1994 - Ledermix was a \$500,000 per year product
 - ➔ Compared to their other drugs - worth \$\$Billions
 - ➔ They did not want to invest in the process for what they perceived was a small market
 - ✧ Despite me trying to persuade them!!



The Ledermix Story

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The Ledermix Story

? Systemic side effects of steroids

- ◆ Abbott - Int Endod J 1992; 25: 189-191
 - Showed insufficient steroid amounts used
 - Insufficient steroid released systemically to have any potential for systemic side effects
 - Compared with endogenous steroid in humans
 - ➔ Normal and under stress



International Endodontic Journal 1992; 25: 189-191

Systemic release of corticosteroids following intra-dental use

P. V. ABBOTT
Dental School, University of Western Australia, Perth, W.A. 6000, Australia

Summary
Concerns have been expressed in the past that the use of corticosteroids within root canal endodontics or pulp capping agents may lead to deleterious systemic effects. Calculations of the highest possible amounts that could be used, plus an analysis of the release and diffusion characteristics, and comparison with known endogenous levels of corticosteroids, reveal that the intra-dental use of Ledermix paste and Ledermix cement is unlikely to result in any systemic side-effects.

Keywords: corticosteroids, endodontics, medicaments, pulp capping.

Introduction
The use of corticosteroids in dentistry was first reported for the treatment of various soft tissue lesions (Epstein et al. 1952) and temporomandibular joint disorders (Epstein et al. 1952; Brown & Lane 1952). Soon after these reports, Willebrand (1954) used a hydrocortisone tooth pulp electroanalgesic of rubber root canals, and he reported that he was able to obtain rapid relief of pain. Subsequently, Schneider (1962) described the materials that are now commercially marketed as Ledermix paste and Ledermix cement (Lederle Pharmaceuticals, Wollschlaeger, Germany). Ledermix paste contains triamcinolone acetonide, an anti-inflammatory agent, at a concentration of 1%, while the cement form contains triamcinolone acetonide at a concentration of 0.67%.

When the Ledermix materials and other similar corticosteroid-containing formulations were commercially released, there was a considerable amount of opposition to their use (Shokard & Harris 1964; Kira et al. 1964; Sater 1965). One of the arguments applied was that the intra-dental use of corticosteroids might result in systemic side-effects which could be harmful to the patient and might interfere with other disease processes. This argument was supported by the results of studies which showed that when hydrocortisone was applied directly to the dental pulp, it could be detected in other body organs within 2 min in humans (De Tora & Ross 1947) and after 10 min in rats (Page et al. 1975).

The actual release of corticosteroids from dental materials to the systemic circulation has not been questioned. However, the amounts that are likely to reach the systemic circulation system following intra-dental use have not been reported in the dental literature. Therefore the following information is presented and is summarized in Tables 1 and 2.

The corticosteroids
The human body produces 20-30 mg of endogenous cortisol per day. In a stress situation this level can

Table 1. Summary of corticosteroid levels

Corticosteroid	Endogenous cortisol in humans
Cortisol in 'stress situation'	20-30 mg day ⁻¹
Cortisol/triamcinolone potency	1:8

Table 2. Summary of calculations

	Ledermix cement	Ledermix paste
Maximum amount of Ledermix used in tooth (mg)	< 100	76.84
Maximum amount of triamcinolone in tooth (mg)	0.57	0.8
(Cortisol equivalent) (mg)	(1.85)	(3.0)
Triamcinolone released after 1 day (mg)	0.26	0.24
(Cortisol equivalent) (mg)	(1.3)	(1.2)

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The Ledermix Story

Table 1. Summary of corticosteroid details

Endogenous cortisol in humans	20–30 mg day ⁻¹
Cortisol in 'stress situations'	300–400 mg day ⁻¹
Cortisol:triamcinolone potency	1:5

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Abbott - Int Endod J 1992; 25: 189-191

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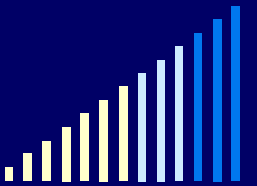
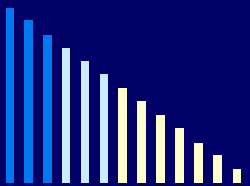
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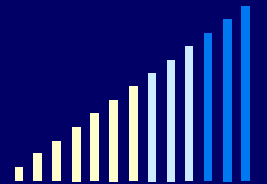
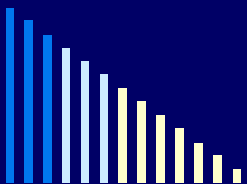
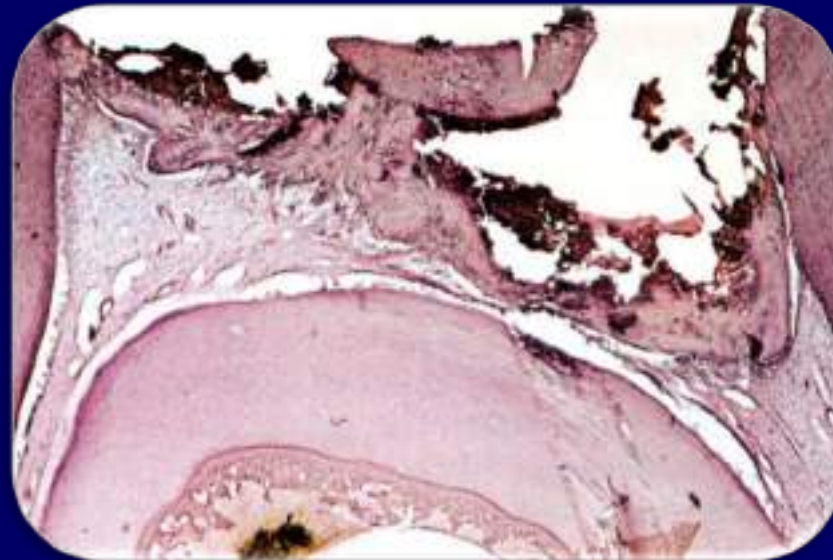


The Ledermix Story

? Inability of steroids to stimulate calcific repair

◆ Mixed reports from histological studies

■ Schroeder 1981



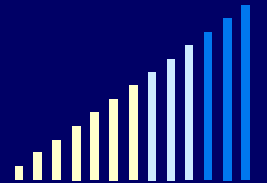
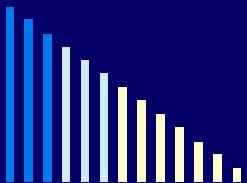
The Ledermix Story

■ Typical healing response - Ledermix Cement

*Schroeder & Triadan 1962; Schroeder 1968, 1972;
Barker & Ehrmann 1969; Barker & Lockett 1971, 1972;
Clarke 1971; Barker 1975; Robertson 1977; Ehrmann 1981; etc.*



- Normal pulp tissue in contact with the cement
- No inflammatory cells
- Occasionally diffuse calcifications in the pulp
- Occasionally a dentine bridge forms



The Ledermix Story

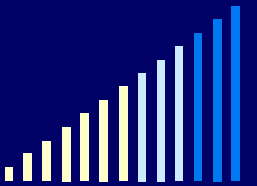
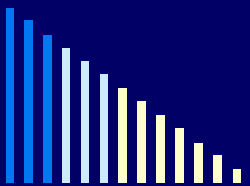
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◆ Mixed reports

◆ BUT - the

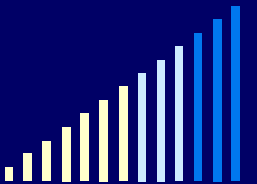
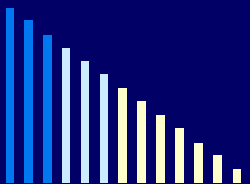
NO !!!

Does it matter if a dentine bridge forms or not ??



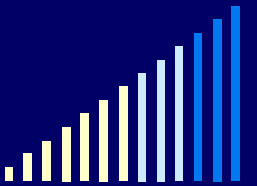
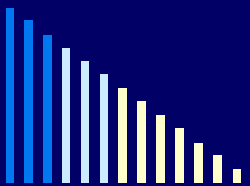
The Ledermix Story

- ◆ What does a dentine bridge do?
 - It just makes dentists “feel good” !!
 - Because we have traditionally been taught that a bridge is essential to indicate healing more FAKE NEWS !!!
 - Indicates the pulp has been irritated and stimulated
 - But this is not essential for healing
 - Dentine bridge provides NO protection for the pulp in the future
 - Porous, lacks usual structure
 - Even normal dentine does not prevent bacterial penetration
 - Once bacteria reach the bridge - it is TOO LATE !!!



The Ledermix Story

- ◆ Some of the concerns were:
 - Systemic side effects of steroids
 - Inability of steroids to stimulate calcific repair
 - Steroids lead to chronic inflammation and/or pulp necrosis
 - Development of tetracycline-resistant micro-organisms
 - Development of hypersensitivity reactions to tetracyclines
 - More specific anti-microbial agents may be available

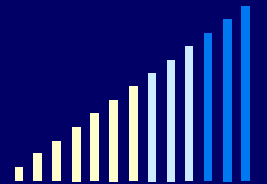
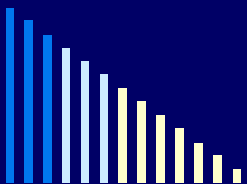
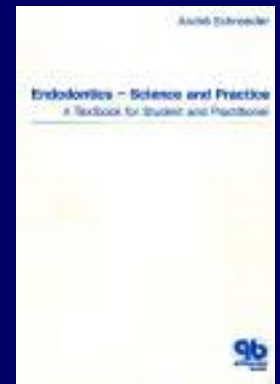
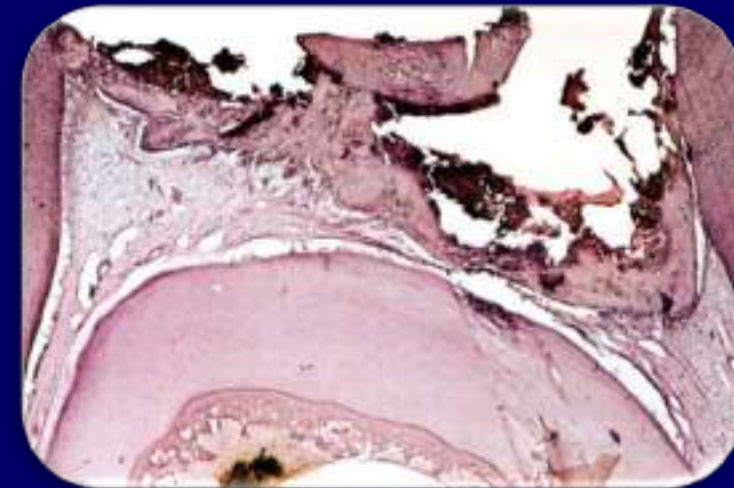


The Ledermix Story

? Steroids lead to chronic inflammation and/or pulp necrosis

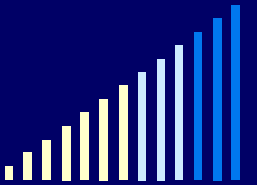
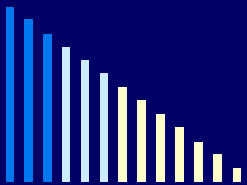
◆ NOT supported by clinical and histological studies

- Schroeder 1981
- And many others



The Ledermix Story

- ◆ Some of the concerns were:
 - Systemic side effects of steroids
 - Inability of steroids to stimulate calcific repair
 - Steroids lead to chronic inflammation and/or pulp necrosis
 - Development of tetracycline-resistant micro-organisms
 - Development of hypersensitivity reactions to tetracyclines
 - More specific anti-microbial agents may be available

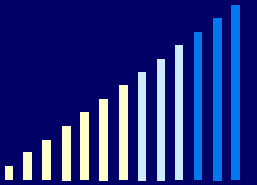
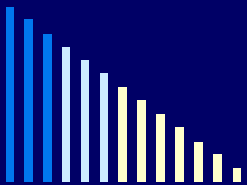


The Ledermix Story

- ? **Development of tetracycline-resistant micro-organisms**
- ◆ **NO reports in the literature after 58 years of use in many countries throughout the world**
 - ◆ **During root canal treatment, do not rely on one medicament**
 - **Recommendations are to use Ca(OH)_2 as a subsequent dressing in all infected canals before doing the root canal filling**
 - if Ledermix paste is used initially
 - **Ca(OH)_2 has broader anti-bacterial spectrum of activity**
 - will destroy any remaining bacteria
 - **Hence, if resistance does occurs, Ca(OH)_2 will counteract it**

The Ledermix Story

- ◆ Some of the concerns were:
 - Systemic side effects of steroids
 - Inability of steroids to stimulate calcific repair
 - Steroids lead to chronic inflammation and/or pulp necrosis
 - Development of tetracycline-resistant micro-organisms
 - Development of hypersensitivity reactions to tetracyclines
 - More specific anti-microbial agents may be available



The Ledermix Story

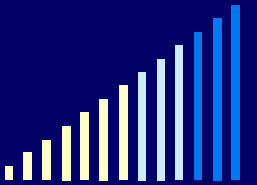
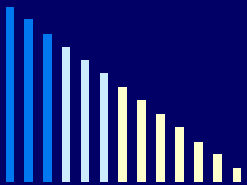
? Development of hypersensitivity reactions to tetracyclines

- ◆ Allergy to tetracycline is extremely rare
- ◆ Only two cases reported over 58 years of use
 1. Letter to Editor - *BDJ* 2013 - very little detail given
 2. Case report
 - Kaufman, Solomonov, Galieva, Abbott
Int Endo J 2014; 47: 1090-1097.
 - ➔ Confirmed tetracycline allergy via skin tests
 - ➔ Patient recovered when Ledermix removed from the tooth



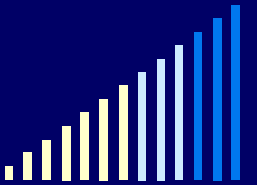
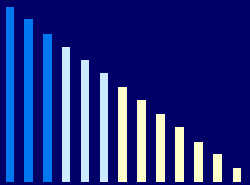
The Ledermix Story

- ◆ Some of the concerns were:
 - Systemic side effects of steroids
 - Inability of steroids to stimulate calcific repair
 - Steroids lead to chronic inflammation and/or pulp necrosis
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 - More specific anti-microbial agents may be available



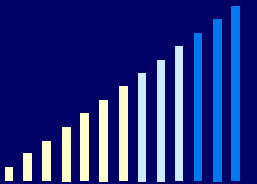
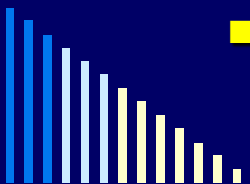
The Ledermix Story

- ? More specific anti-microbial agents may be available
- ◆ Ehrmann (1981) stated inclusion of a tetracycline was “*most unfortunate*”
 - Believed a bacteriocidal agent is better than a bacteriostatic agent
 - However it is not essential to kill all bacteria
 - As long as they cannot reproduce, they will not survive
 - Other treatment strategies should also be used to make the environment within the root canal system unfavourable for bacterial survival
 - ✧ e.g. remove caries, cracks, restorations, etc.



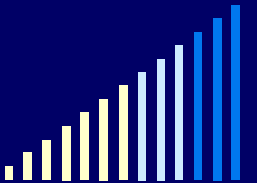
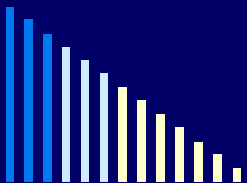
The Ledermix Story

- ? More specific anti-microbial agents may be available
- ◆ Many other antibiotics have been suggested and/or tested
 - None have proven to be any better in the root canal system
- ◆ All AB's have limited spectrum of activity
 - Root canal infections are multi-species
- ◆ Need caution:
 - Resistance more common as other AB's are more commonly used systemically for many conditions
 - Allergy to penicillins preclude their use



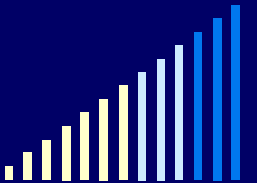
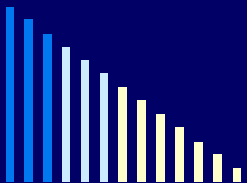
The Ledermix Story

- ? More specific anti-microbial agents may be available
- ◆ There is no “perfect” antibiotic
- ◆ During root canal treatment, must not rely on one medicament
 - Recommendations are to use Ca(OH)_2 as a subsequent dressing in all infected canals before doing the root canal filling
 - if Ledermix paste is used initially
 - Ca(OH)_2 has broader anti-bacterial spectrum of activity
 - will destroy any remaining bacteria
 - Hence, if resistance does occurs, Ca(OH)_2 will counteract it



The Ledermix Story

- ? More specific anti-microbial agents may be available
- ◆ Ehrmann (1981) stated inclusion of a tetracycline was “*most unfortunate*”
- ◆ However, subsequent studies on resorption have shown the choice of a tetracycline was actually **VERY FORTUNATE !!**
 - Due to tetracycline’s ability to inhibit clastic cells
 - Especially useful for inflammatory resorption
 - Prevention and Interceptive treatment

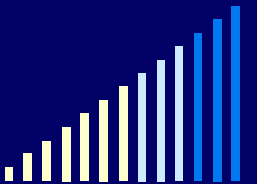
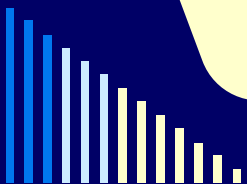


The Ledermix Story

◆ Some of the concerns were:

- Systemic side effects of steroids
 - Inability of steroids to stimulate bone growth
 - Steroids lead to chronic osteomyelitis and bone necrosis
 - Development of resistance in organisms
 - Development of alternative agents to tetracyclines
- agents may be available

**NONE of these concerns were valid in the 1960's
..... and they are still NOT valid today !!!**



Ledermix Cement Schroeder (1962)

- *C-st:* Triamcinolone - 0.67 %
- *Ab:* Demeclocycline - 2.0 %
- Calcium hydroxide - 33.4 %
- Zinc oxide - 47.2 %

Powder



+ Eugenol - 85% of the liquid

→ Forms a hard-setting cement when mixed

Ledermix Cement

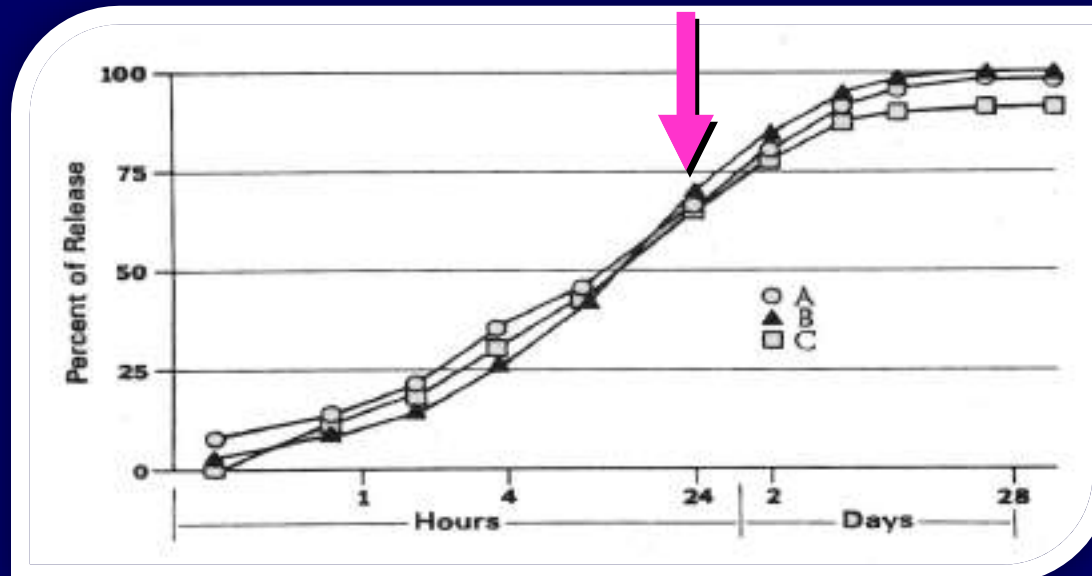
- Triamcinolone - 0.67 %
- Calcium hydroxide - 33.4 %
- Zinc oxide-eugenol - 47.2 %

◆ Triamcinolone

■ Anti-inflammatory agent

→ *In vitro* - 70% is released by the end of day 1

→ Rest by the end of day 3 (Hume & Kenney - JoE 1981)



Ledermix Cement

- Triamcinolone - 0.67 %
- Calcium hydroxide - 33.4 %
- Zinc oxide-eugenol - 47.2 %

◆ Triamcinolone

■ Anti-inflammatory agent

→ *In vitro* - 70% is released by the end of day 1

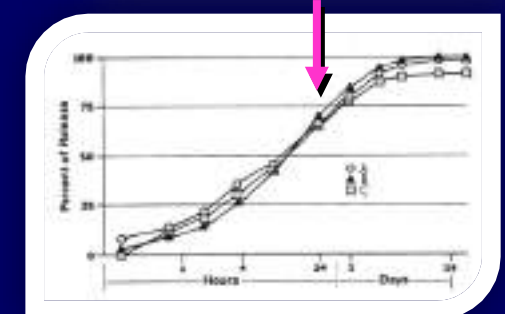
→ Rest by the end of day 3 (Hume & Kenney - JoE 1981)

■ Expect this to be much faster when In Vivo

→ i.e. In a tooth with pulp blood flow

→ Due to the dynamics of diffusion and clearance

■ Hence: *there is only a very short term application of triamcinolone*



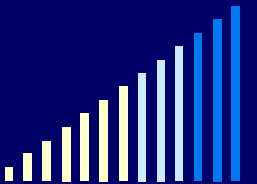
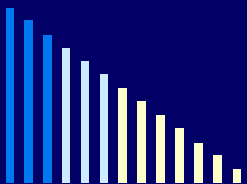
Ledermix Cement

- Triamcinolone - 0.67 %
- Calcium hydroxide - 33.4 %
- Zinc oxide-eugenol - 47.2 %

◆ Triamcinolone

- *Hence: there is only a very short term application of triamcinolone*
- *There is NO evidence that it causes pulp necrosis without symptoms*

- ➔ *A long held misconception about Ledermix Cement*
- ➔ *Arose from inappropriate use, lack of diagnosis, poor understanding of disease processes, poor understanding of pharmacodynamics of CS, misconceptions about CS, unrealistic expectations of the material, etc.*



Ledermix Cement

- Triamcinolone - 0.67 %
- Calcium hydroxide - 33.4 %
- Zinc oxide-eugenol - 47.2 %

◆ Triamcinolone

- Anti-inflammatory agent (1-3 days maximum effect)

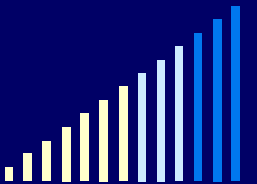
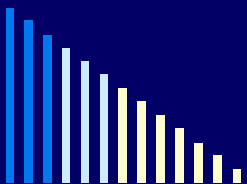
◆ Calcium hydroxide

- Promotes dentine repair (numerous studies)

◆ Zinc oxide - Eugenol

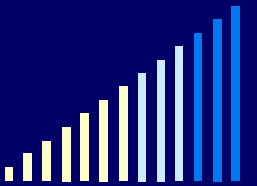
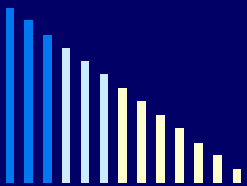
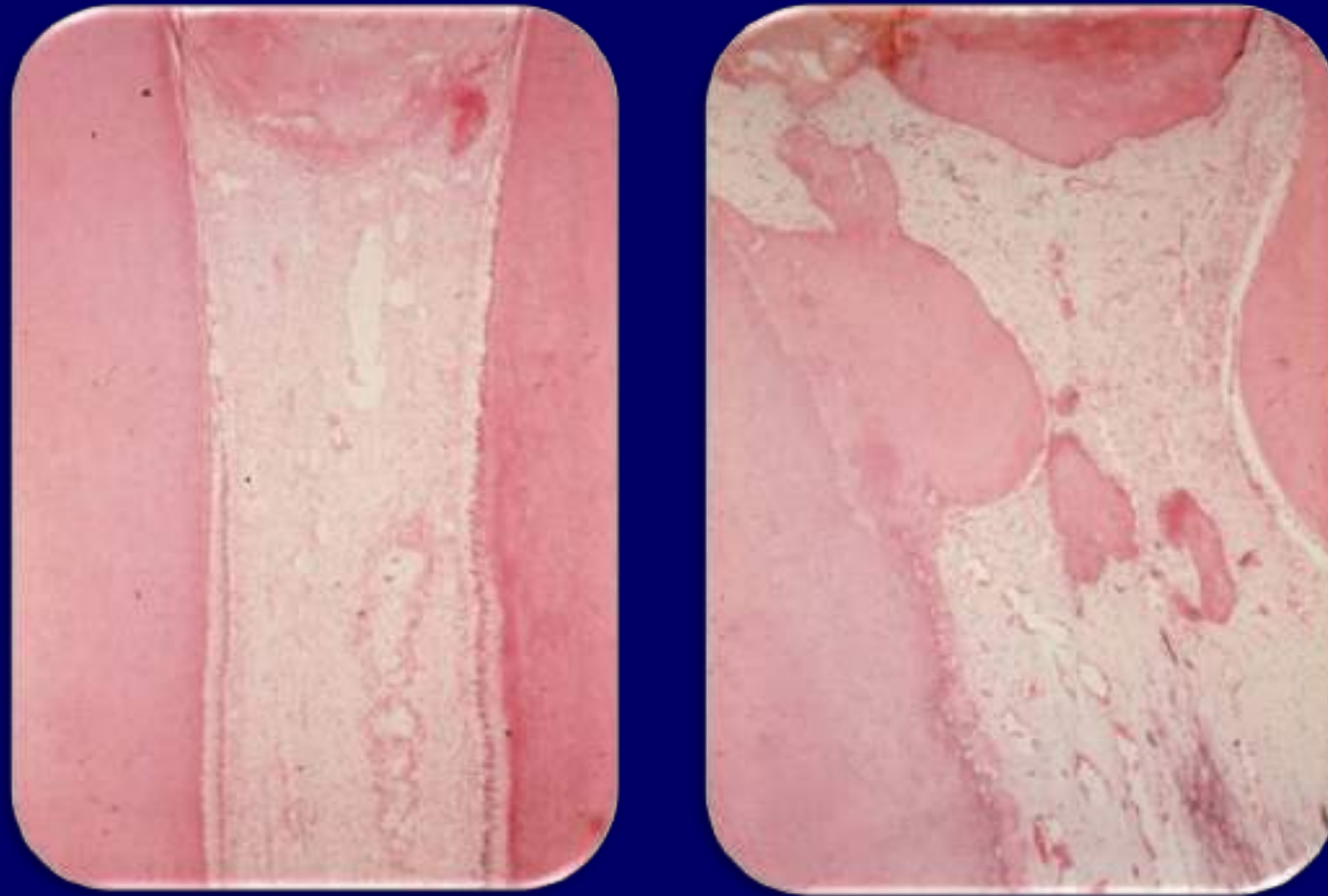
- Anti-inflammatory and anti-bacterial

(Brannström 1979, Schroeder 1981, Hume 1984, 1986, 1987)



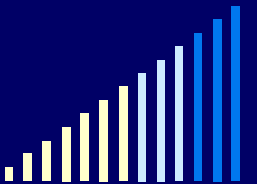
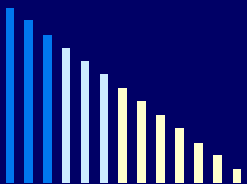
Typical healing response - Ledermix Cement

Robertson 1977

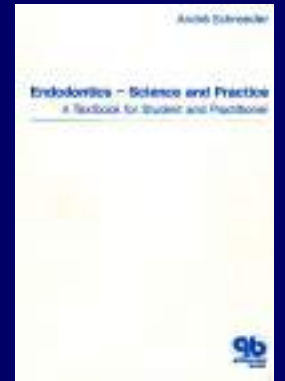


Human Pulp Reactions to a Glucocorticosteroid-Antibiotic Compound

Barker BC, Ehrmann EH. *Aust Dent J* 1969; 14: 104-19



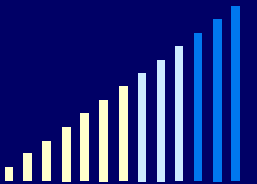
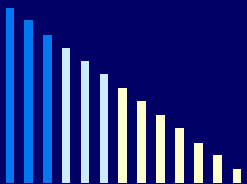
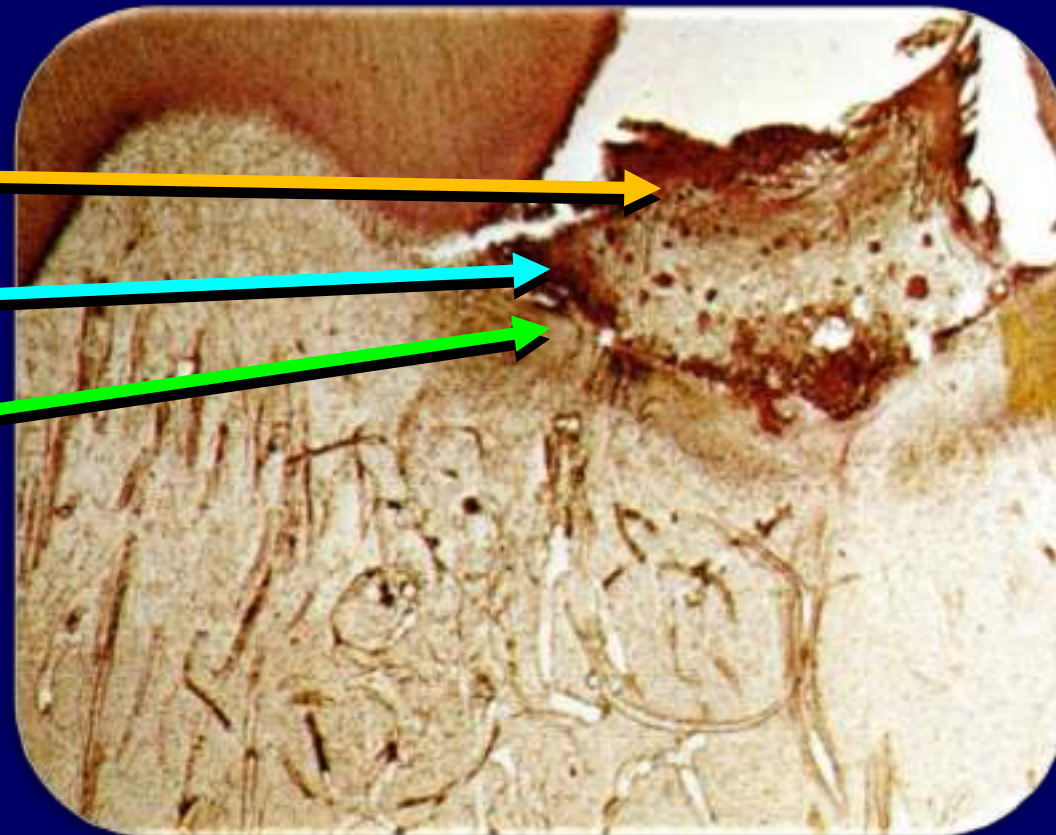
- Typical healing response with Ca(OH)_2
(Schroeder 1981)



Necrosis

Calcified tissue

Dentine bridge



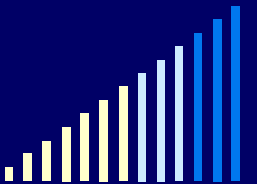
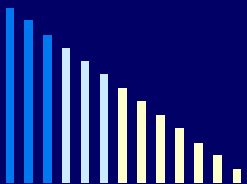
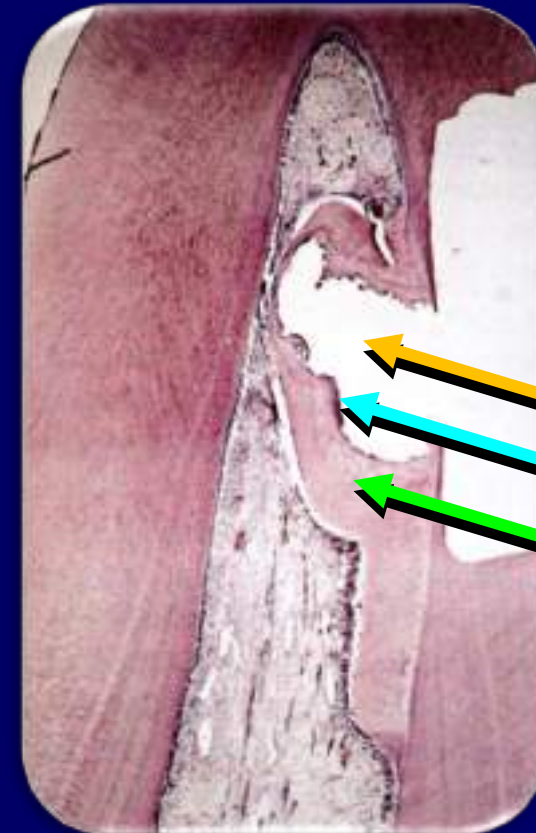
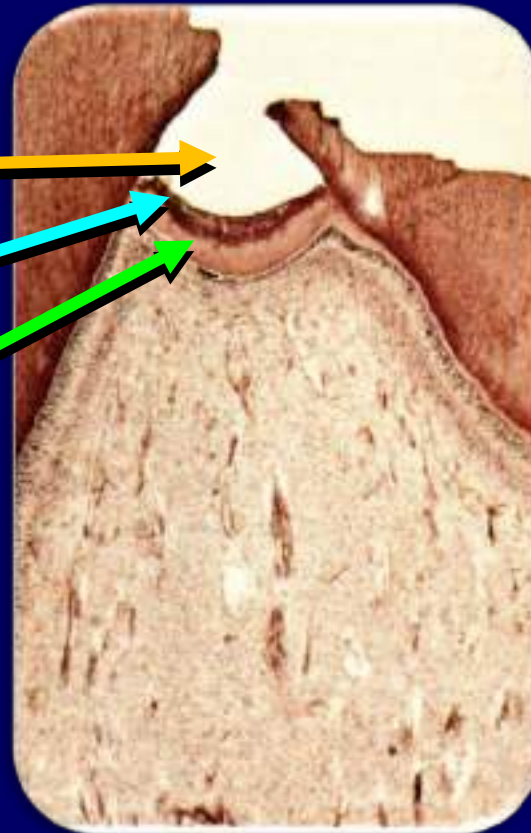
- Typical healing response with $\text{Ca}(\text{OH})_2$
(Schroeder 1981)



Necrosis

Calcified tissue

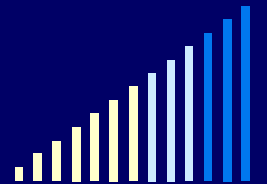
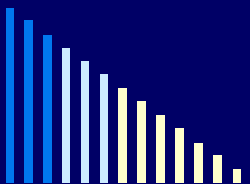
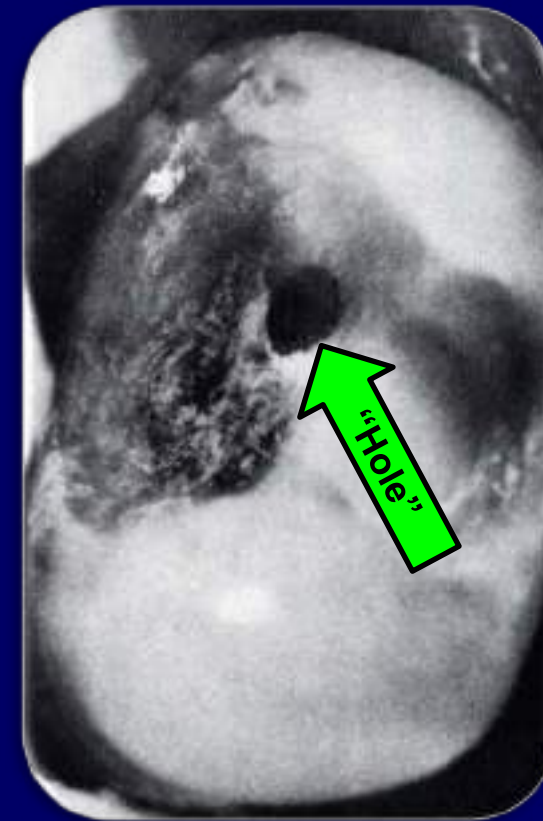
Dentine bridge



■ Typical healing response with Ca(OH)_2

(Schroeder 1981)

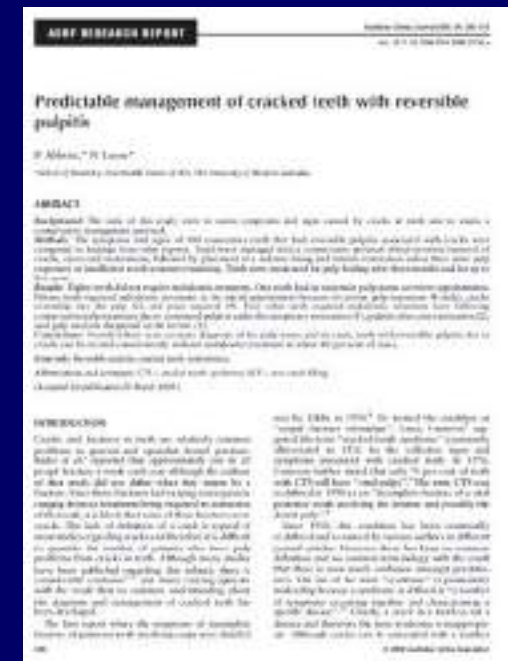
- Dentine “bridge” forms below the exposure site
- The necrotic layer manifests as a “hole” if the tooth is re-entered later



Predictable Management of Cracked Teeth with Reversible Pulpitis

Abbott PV, Leow N.

Aust Dent J 2009; 54: 306-315.

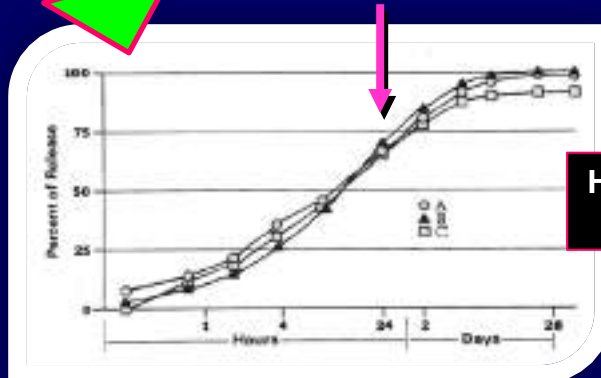


Cracked Teeth with Reversible Pulpitis – Abbott & Leow *ADJ* 2009

- ◆ 85 teeth - Reversible pulpitis symptoms resolved

Ledermix Cement

■ Immediately	71 %
■ 1 day	21 %
■ 2 days	6 %
■ 3 days	3 %
	<u>100 %</u>



Hume & Kenney
JoE 1981



Cracked Teeth with Reversible Pulpitis – Abbott & Leow *ADJ* 2009

Summary

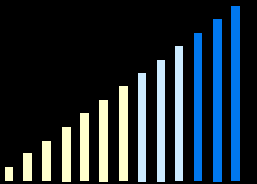
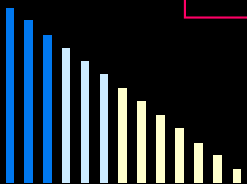
85 teeth managed conservatively with Ledermix Cement & GIC interim restoration

- Pulp recovered 80 teeth (94.0%)
- Pulpitis continued 1 tooth (1.2%)
- Pulp necrosis at 3 mths 1 tooth (1.2%)
- Pulp status uncertain 1 tooth (1.2%)
- Pulpitis after core 2 teeth (2.4%)

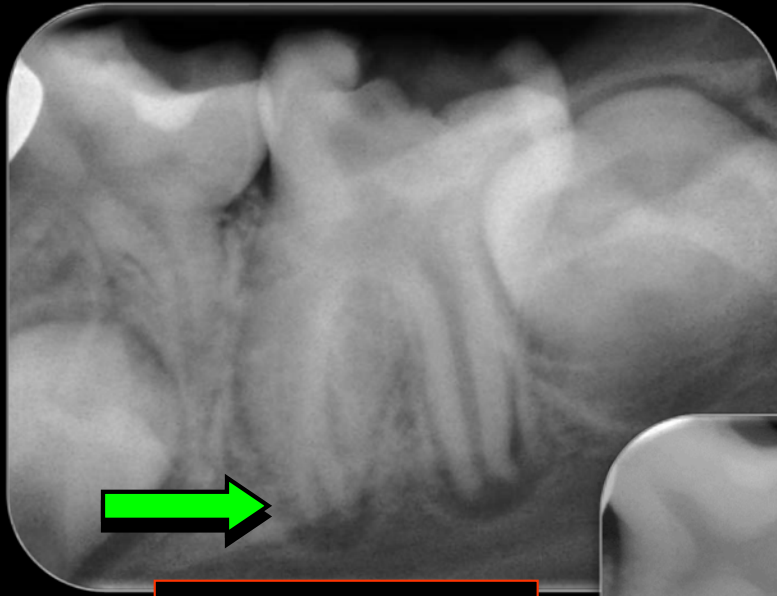


Ledermix Cement - Partial Pulpotomy

Tooth 11



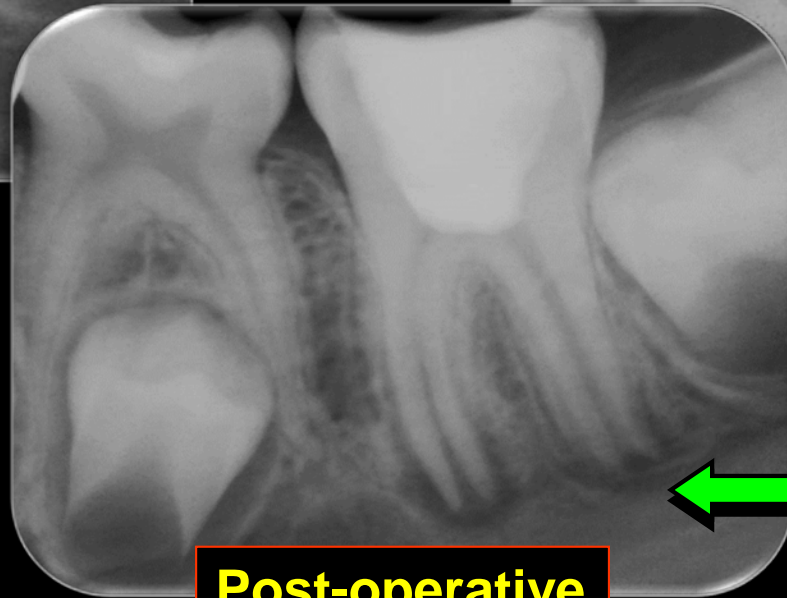
Ledermix Cement - Pulpotomy



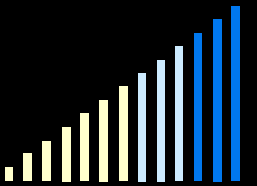
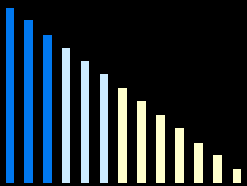
Pre-operative



1 year



Post-operative



Conservative Pulp Treatment

- *What materials can / should we use?*

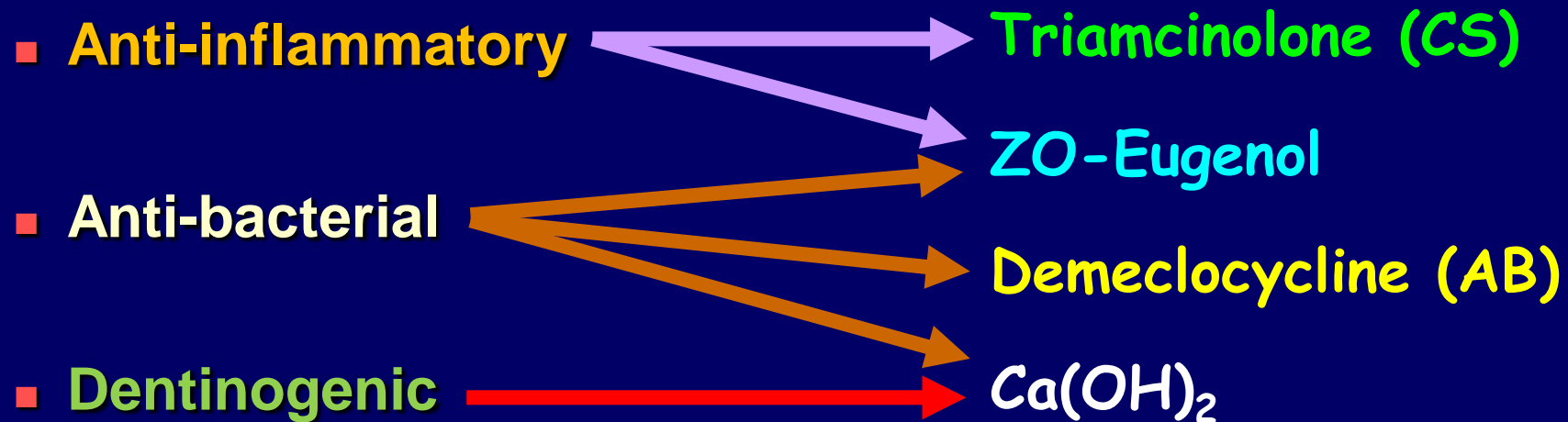
CHOICES:

- 
1. **Corticosteroid / Antibiotic cement**
 2. Calcium hydroxide
 3. Bioceramic materials
(e.g. MTA, Biodentine, etc)
- 



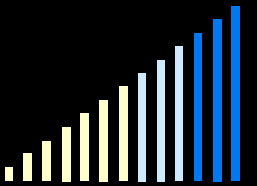
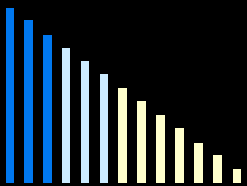
Ledermix Cement

- ✓ Meets the THREE criteria required for an ideal pulp capping and pulpotomy material (Schroeder 1962, 1981)



36: Pulpless, infected root canal system with chronic apical periodontitis due to breakdown of the restoration

37: Acute irreversible pulpitis due to restoration breakdown and caries



Ledermix Paste

- ◆ Triamcinolone - 1%
- ◆ Demeclocycline - 3%

In a water soluble paste of:

- Triethanolamine NF
- Calcium chloride USP
- Zinc oxide
- Sodium sulphite (anhydrous)
- Polyethylene glycol 4,000 USP
- Distilled water



Barriers to diffusion of Ledermix® paste in radicular dentine

Melissa P.J. Howe MR, Heather G. Bardsley DSc, Barbara De Thomassen FRD
School of Dental Sciences, Cardiff University, Cardiff, South Wales CF10 1TD, UK
© 2005 Blackwell Publishing Ltd, *Journal of Oral Rehabilitation* 32; 689–694

Abstract Twelve extracted human single-rooted teeth with a single root canal were used to study the effects of Z-trigeneration and the effect of cementation on the diffusion of various neutral and anesthetic marker molecules from Ledermix® paste placed in the pulp space. An irrigation regime that combined the use of 15% EDTA and 5% NaOCl resulted in a significant increase in the permeation of the trace molecules through dentine compared with teeth that were irrigated with buffered solution. Mechanical removal of the cementum also resulted in a significant increase in the permeation of the trace molecules. This study demonstrated that neither the cement layer nor the cementum were complete barriers to diffusion. The data obtained appeared to be of clinical relevance and provided further understanding of the dynamics of drugs in tooth roots.

Key words: barrier, diffusion, dentin, drug delivery, irrigation, root canal treatment, sealer, zinc phosphate cement.

Introduction

Dentine can be regarded as a diffusion barrier because of its relatively impermeable mineralized matrix permeated by numerous, tortuous cylindrical water-filled tubules [1]. Diffusion of molecules through enamel dentine has been carefully quantified in a number of studies [1–4] and the effects of a group factor affecting diffusion have been reported [2, 3].

Studies of dentine permeability have generally been performed on extracted teeth using denture alloys or stainless steel discs. A comparison of *in vivo* and *in vitro* permeability of dentine indicated that the rates were very similar and substances placed on intact dentine were rapidly detected extrorally [5]. Permeation time had little effect on permeability *in situ* [6].

The major factors affecting dentine permeability appear to be the size of the molecule being moved [7, 8], and the nature of the dentine surface in contact with the substance [1, 8, 9]. With respect to molecular size, the rates of permeation were directly related to the molecular dimensions, with smaller molecules permeating more rapidly [2, 8]. The charge of ions did not affect permeation [2]. Noting the nature of the dentine surface altered the permeability of the dentine, highly polished and etched dentine surfaces showed different rates of etched-dentine [2]. Other studies [6, 7] have

confirmed the effects of acid-etching. This increase in permeability is due to removal of surface debris including the tubules [7].

Rose dentine is similar in structure to coronal dentine and it appears that it has similar diffusion characteristics. A recent study [8] reports the diffusion patterns of zinc tetrachloride, a conventional and demethylchloxyethylene dimethacrylate, a non-toxic adhesive, through human tooth root canals. There was 2 mm penetration at the apical components of Ledermix® paste, a composite flowpaste approved in several parts of the world for the treatment of pulpal and periapical disease. The placement of the paste in the root canal space has been observed to increase the efficacy of treatments of periapical infections [9, 10] and to help to reduce the incidence of inflammation in the periodontal ligament [11, 12].

Mechanical instrumentation of root canals has been shown to produce a smear layer on the dentine walls. This smear layer has been shown to be at atmospheric level of debris, primarily calcium hydroxide, that blocks the dentinal tubules [13, 14]. The dentinal tubules may harbor bacteria as a consequence of pulp infection, occlusion of these tubules is a prime objective of endodontic therapy [15].

This study aimed to determine whether a dentine permeability parameter is affected by various che-

Abstract • Hesse W, Hildebrand G. Barriers to diffusion of Listeria in agar in radial-ridge media. *Environ Dev Transm* 2005; 4: 380–384.

Summary • Freshly extracted human single-tooth swabs with a moist agar surface were used to study the effects of 2 irrigation regions and the effect of cementation on the diffusion of ceftriaxone and azithromycin tracer molecules from Listerium's paste placed in the jugal space. An irrigation region that contained use of 15% EDTAC and 1% NaOCl resulted in a significant increase in the permeability of the agar surface. The results were compared with those that were irrigated with NaCl/saline solution. Mechanical removal of the cementum also resulted in a significant increase in the permeability of the agar surface. The results demonstrated that neither the outer layer nor the cementum were complete barriers to diffusion. The data obtained from this study may be used to help develop a further understanding of the dynamics of drugs in tooth roots.

Key words: radial-ridge (diffusion); tracers; cement; ceftriaxone; azithromycin; single-tooth swabs

© 2005 Wiley Periodicals, Inc. J Biomed Mater Res Part B: Appl Biomater 75B: 380–384, 2005

Keywords: diffusion; barrier; cement; Listerium

1

**Endodontics
& Dental
Traumatology**

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Abbott PV, Heithersay GS, Hume WR. Release and diffusion through human tooth roots *in vitro* of corticosteroid and tetracycline trace molecules from Ledermix® paste. *Endod Dent Traumatol* 1988; 4: 55-62.

Abstract. The release of corticosteroid and antibiotic tracer molecules in Ledermix® paste from the pulp space to the external environment of human tooth roots was determined *in situ*. Fluorescein-labeled tetracycline (one of the tracers) was released through the root canal in a dose-dependent manner. The release of the tracer was lowest after one-third of the tracer left the dentures via the apical foramen; the remainder exited via the dentine. The rate of release of the tracers was highest during the first day, and declined exponentially with time thereafter. After 14 weeks, 98% of tetracycline-labeled tracers had been released. The release of the tracers examined, diffusion rate was not related to the age or sex of the donor. Total release of the tracers was directly related to the area of contact between the paste and dentine. The data obtained are of use to the dental profession and to our general understanding of drug dynamics in tooth roots.

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Adelaide, Australia

Dr. P. V. Abbott, Lincoln House, 4 Wertheim Ave.,
West Perth 6009, Australia.

There are at present few quantitative data on the movement of drugs and chemicals out of the root canal space into the periradicular or periodontal environment. However, a few studies have been carefully conducted in order of assessing the dentine behaves as an impermeable solid traversed by water-filled tubules (4). It may be assumed that the dentine is a solid with some of the same characteristics. However, the possibility also exists of diffusion out of the root canal via the apical foramina, and the balance between the 2 diffusion paths is of relevance to considerations of both drug therapy and toxicity.

In this work we chose to examine the local availability of the active components of Lederer's paste, a well-known eugenic agent, in the treatment of pulpitis of the world in the treatment of pulpitis and periapical disease. The paste has two active components, triamcinolone (a corticosteroid) and demeclocycline (a tetracycline antibiotic). The placement of the paste in the root canal space appears to add to the efficacy of the use of demeclocycline (5, 6), and it has been reported to reduce the incidence of root resorption (7).

Abbott PV, Hume WR, Heithersay GS. Effects of combining Ledermix® and calcium hydroxide pastes on the diffusion of a tetracycline and tetracycline through human tooth roots *in vitro*. *Endod Dent Traumatol* 1989; 5: 188-192.

Abstract - A 50:50 mixture of a corticosteroid/antibiotic paste and calcium hydroxide has been used clinically as a root canal dressing agent. This study investigated the effect on the release and diffusion of the corticosteroid and antibiotic components of Ledermix® paste when it was mixed with a calcium hydroxide-methyl cellulose paste. The release rates of the two molecules were lower when the mixture was used compared to release from Ledermix alone. The results indicated that this combination of materials, when used a long-term intracanal dressing, was likely to be more effective than Ledermix alone.

**Paul Vincent Abbott, Wyatt Roderic
Rame, Geoffrey Sinclair Rutherford**
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Accepted for publication January 21, 1993

[illegible]

10

The release and diffusion through human

coronal dentine *in vitro* of triamcinolone and demeclocycline for Ledermix® paste

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David F. TREMPER ¹

¹ School of Dentistry, University of Leeds, Leeds LS2 9JT, UK
² School of Dentistry, University of Manchester, Oxford Road, Manchester M13 9PL, UK

Abstract – X-ray microanalysis of extracted human third molars with some sections of the root free of dentine revealed that coronal and anesthetic tracer molecules from Ledermix® paste used as an indirect pulp-capping agent were released from the root surface, followed through dentine and reached a peak rate of diffusion at 2 h. The rate of diffusion of the anesthetic tracer was significantly greater than that of the steroid. The release of the steroid was reduced by the contraction of the dentin in the denture were calculated; thus showed that a gradual release from the cavity free to the pulp was the main mode of release. The release of the anesthetic tracer and helped explain the therapeutic benefits of this medicament when used as an indirect pulp-capping agent.

Keywords: demeclocycline, diffusion, indirect pulp-capping, triamcinolone.

Introduction

Ledermix® paste is a compound therapeutic agent used in several parts of the human in the treatment of pulpitis. It contains an anesthetic, tetracycline, an active component, triamcinolone (a corticosteroid), and demeclocycline (hydroxy demeclocycline, a tetracycline antibiotic) (1). The antibiotic component is present in concentrations of 10% and 25%, respectively. The remaining components were a water soluble chain carrier, a buffer and an emulsifier (2).

Many authors (3–7) have observed the clinical effectiveness of Ledermix® paste in the treatment of either direct or indirect pulp-capping agents in rubber dam pulp inflammation and pain. There are a number of reasons that explain the clinical success of this material.

Firstly, the corticosteroid is a similar agent to that is contained in triamcinolone and demeclocycline. However, this is not the case with the anesthetic component, hard-setting base and in lower concentrations (8, 9), and 25%, respectively, than is the paste used as an indirect pulp-capping agent.

Secondly, the release of the anesthetic tracer and

the steroid paste has been investigated (10, 11); the triamcinolone was released into the pulp of the root of the first 3 h after application of the paste during the following five days. The study showed that triamcinolone readily diffused through dentine and reached the pulp providing a minimal barrier to diffusion.

Diffusion of various molecules through coronal dentine has been questioned in a number of studies (12–15). The authors have questioned the presence of a concentration gradient through the dentine because of the contraction of the pulp has been demonstrated to cause tissue shrinkage.

There have been attempts to quantify the release and diffusion of the active components of Ledermix® paste through coronal dentine, and to determine the availability of these materials to the pulp tissue.

Materials and methods

The method of Hancox (7) was used to treat root

© 1995 Blackwell Science Ltd, *Journal of Oral Rehabilitation* 22: 117–121

The release and diffusion through human coronal dentine *in vitro* of triamcinolone and demeclocycline from Ledermix® paste

Abstract - Grown from a fully extracted human third molar, teeth were used to quantify the release and diffusion of corticosteroid and antibiotic tracer molecules from Lefornix® paste used as an indirect pulp-capping agent. These molecules readily diffused through dentine and reached a peak rate of diffusion at 2 h. The rate then decreased exponentially with time. The concentrations of the drugs in the dentine were calculated, and showed a gradient existed from the drug closest to the pulp space. The data appeared to have clinical relevance and helped explain the therapeutic benefits of this medication when used as an indirect pulp-capping agent.

[illegible]

Material and methods

The method of Hume (22) was used to measure the diffusion of the components of *Ledermyx* paste through coronal dentine. Tritium-labelled $^3\text{H-CT}$

Paul Vincent Abbott, Wyatt Roderic Rama, Geoffrey Sinclair Neillmaray
School of Dentistry, University of Adelaide, Adelaide, Australia

Key words: pulp, diffusion, therapeutic, transcorneal, dimethylsulfoxide.

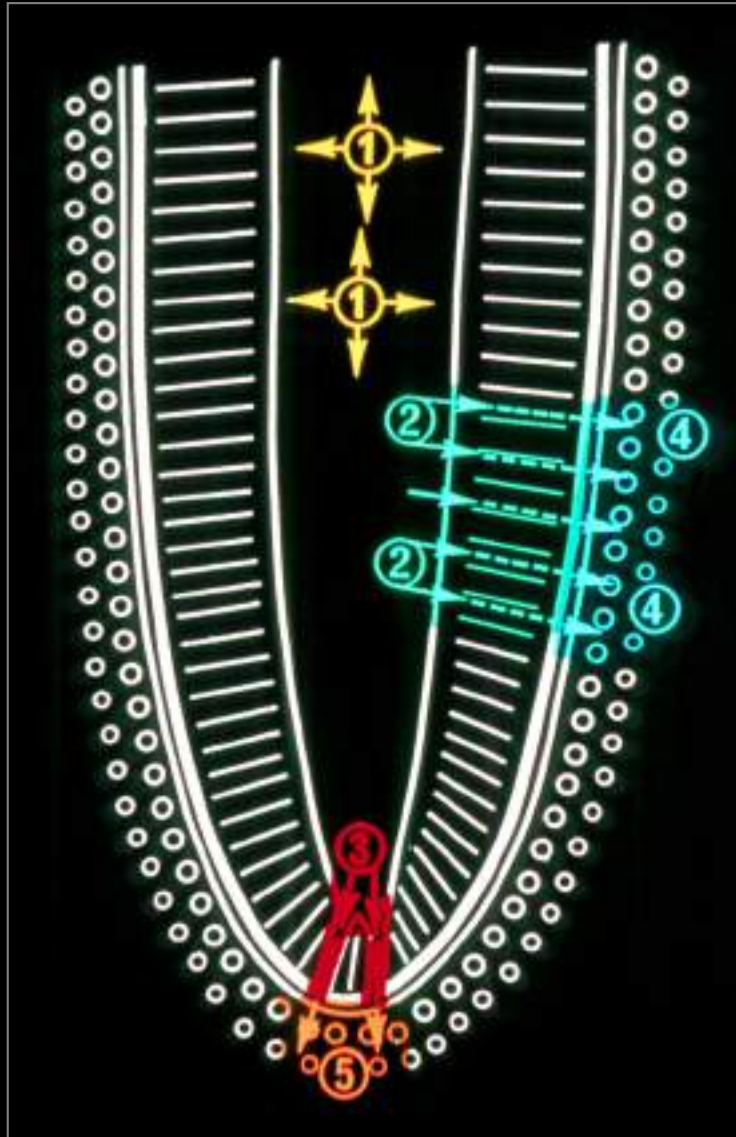
palp-capping agent has been investigated [18, 79], of the transimide was released into the pulp space during the first 24 h and most of the remainder was released during the next 24 h. It was concluded that transimide release diffuses through dentine and that the dentine provides only a minimal barrier to diffusion.

Various monomers and various molecules through coronal dentine have been quantified in a number of studies; these reports have shown that dentine behaves as a barrier to the diffusion of a wide range of molecules [19–22]. The concentration of medicaments within dentine has been quantified and the presence of a concentration gradient through to dentine has been observed [23–25] and the pulp has been confirmed to exist [26–28].

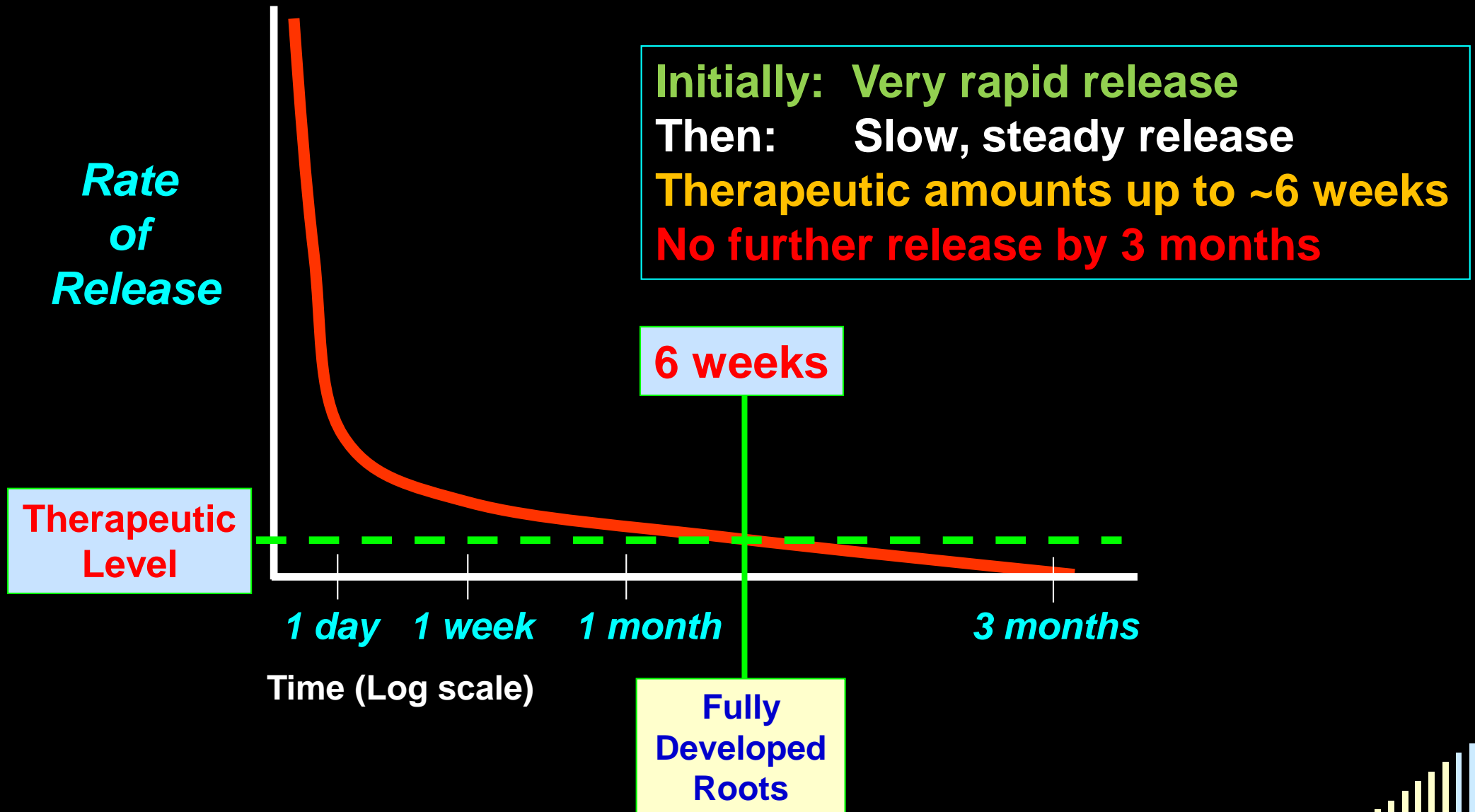
This study was undertaken to quantify the release of dentine from a zinc phosphate cement restorative mix paste through coronal dentine when the paste is used as an indirect palp-capping agent, and to determine the availability of these materials to pulp tissue.

Material and methods

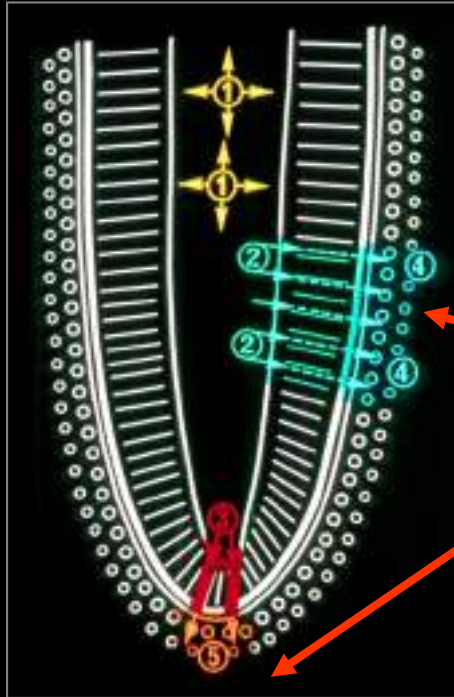
Ledermix paste – Release and Diffusion *Abbott et al EDT 1988, 1989*



Ledermix paste – Release and Diffusion *Abbott et al EDT 1988, 1989*

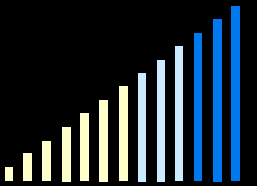
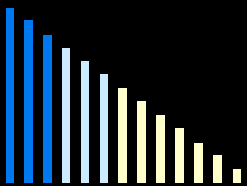


Ledermix paste – Release and Diffusion *Abbott et al EDT 1988, 1989*



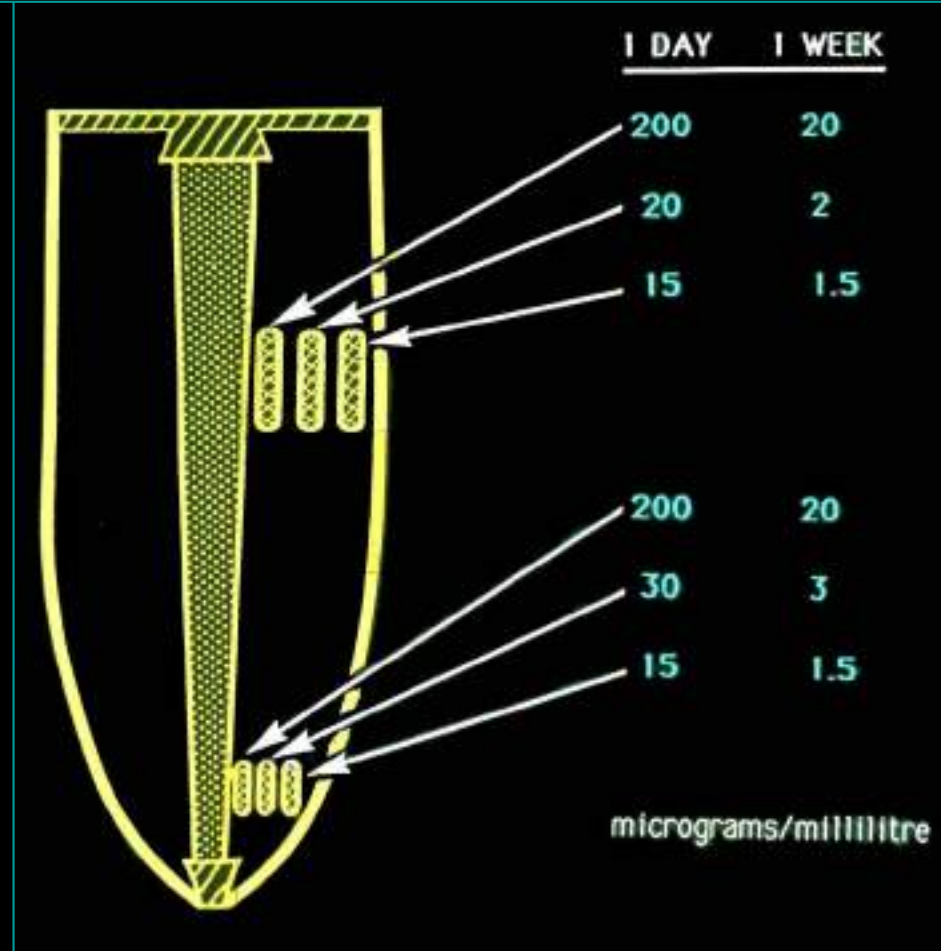
Triamcinolone (Corticosteroid)

- ◆ **Measured peri-radicular concentration**
 - Detected in the nanomolar range
- ◆ *Sufficient for anti-inflammatory action*



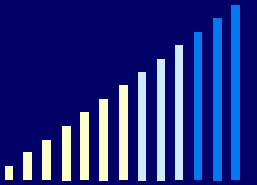
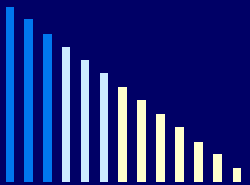
Ledermix paste – Release and Diffusion *Abbott et al EDT 1988, 1989*

Concentrations of **Demeclocycline** in root dentine after Ledermix paste has been applied within the root canal



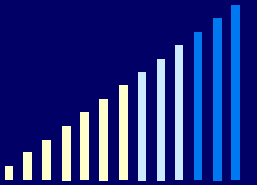
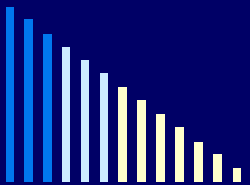
Why Use Medicaments ?

- ◆ **Anti-bacterial action**
 - Residual bacteria in canals, tubules, fins, etc
 - Contaminants between visits
 - Periapical region
 - Periodontal tissues
- ◆ **Reduce periapical inflammation**
- ◆ **Prevent or reduce pain**
- ◆ **Stimulate periapical repair**
- ◆ **Prevent or inhibit inflammatory resorption**



Why Use Medicaments ?

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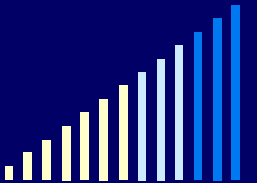
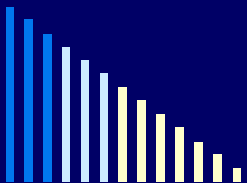
The relationship of intracanal medicaments to postoperative pain in endodontics

Int Endod J 2003; 36: 868-875

E. H. Ehrmann, H. H. Messer & G. G. Adams

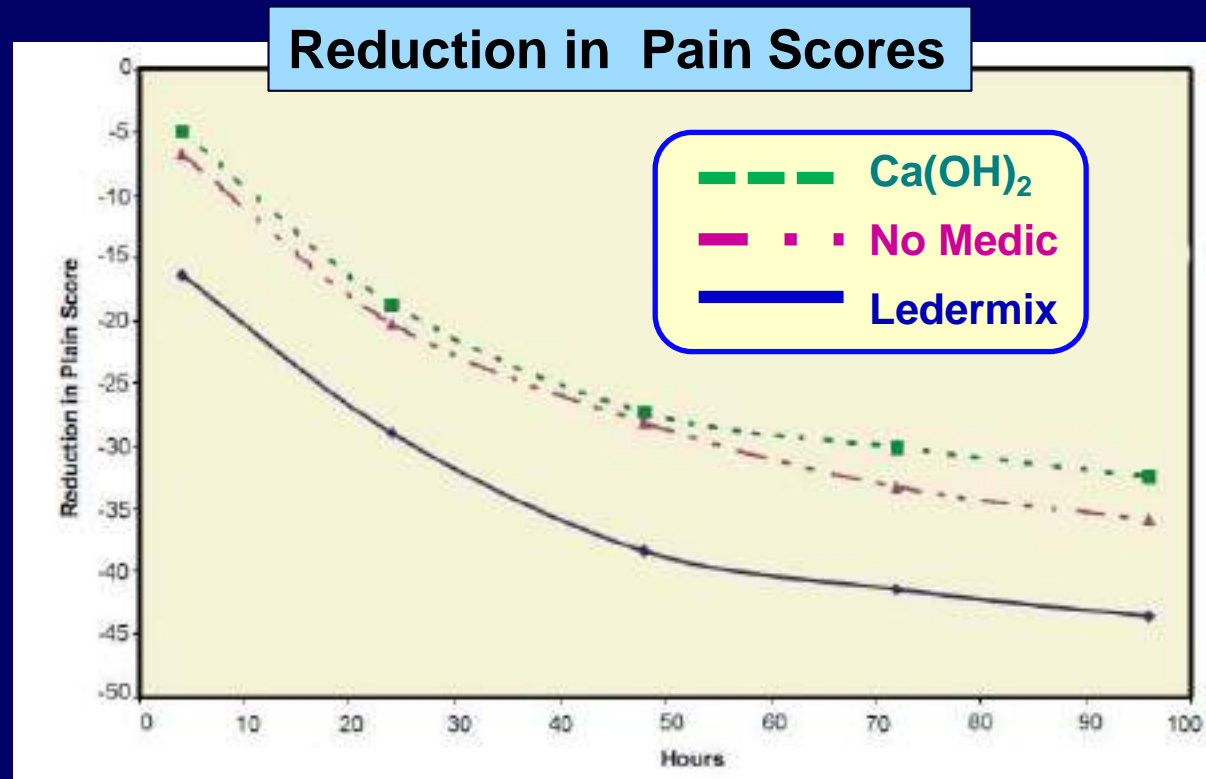
School of Dental Science, Faculty of Medicine, Dentistry and Health Sciences, The University of Melbourne, 711 Elizabeth Street, Melbourne, Victoria, 3000, Australia

- ◆ **223 teeth** - infected root canals with acute apical periodontitis
- ◆ **Root canals instrumented “to the apices”**
 - 1% NaOCl + 15% EDTAC
- ◆ **Ledermix paste, Ca(OH)_2 or no dressing**
- ◆ **Pain scores: Pre-op and for next 4 days**



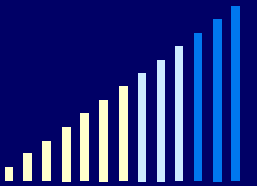
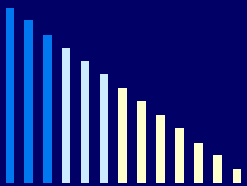
Post-op Pain + Medicaments Ehrmann *et al* - IEFJ 2003

- ◆ **Ledermix group:** Significantly less post-operative pain than the Ca(OH)_2 group and the control group

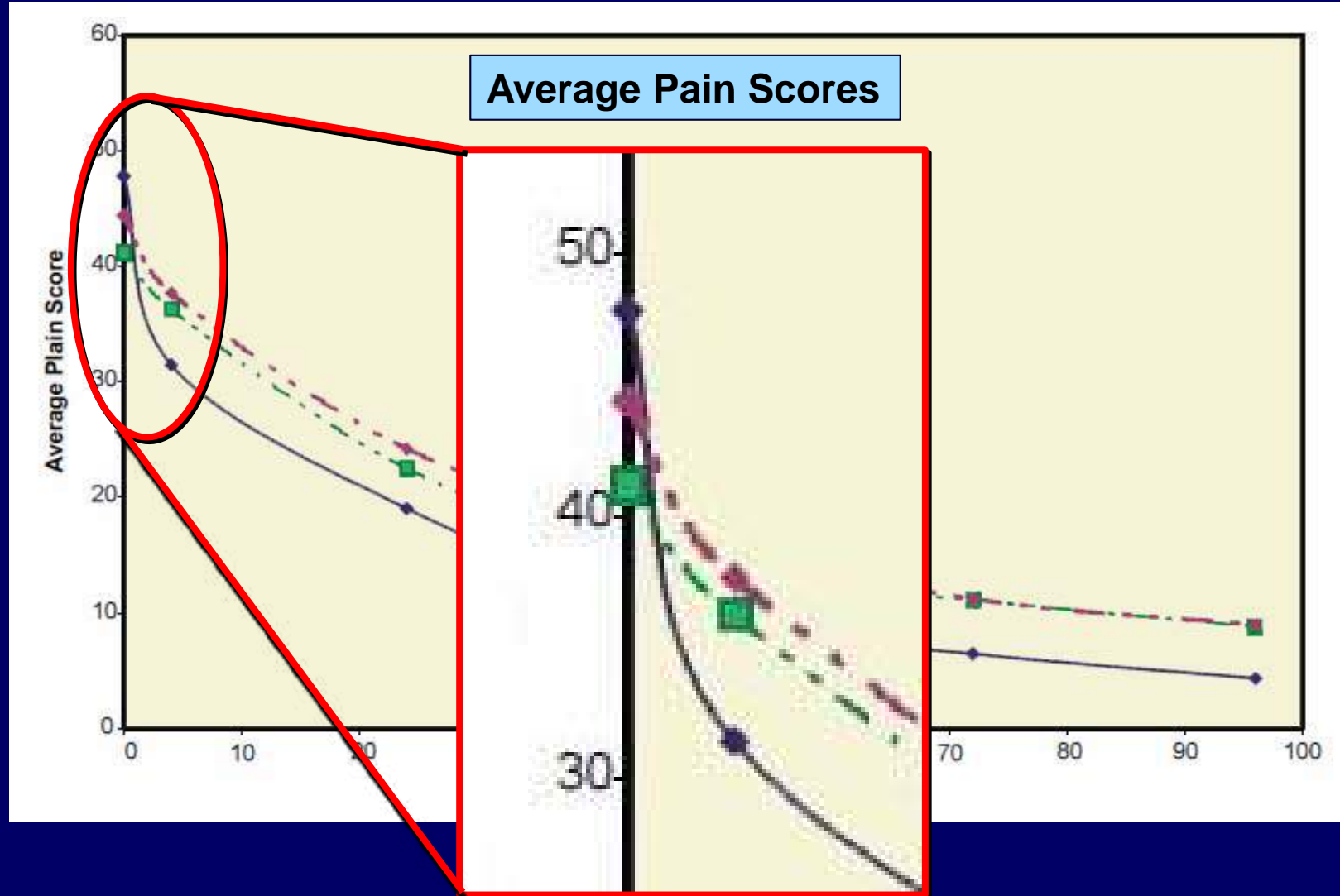


Post-op Pain + Medicaments Ehrmann *et al* - IEJ 2003

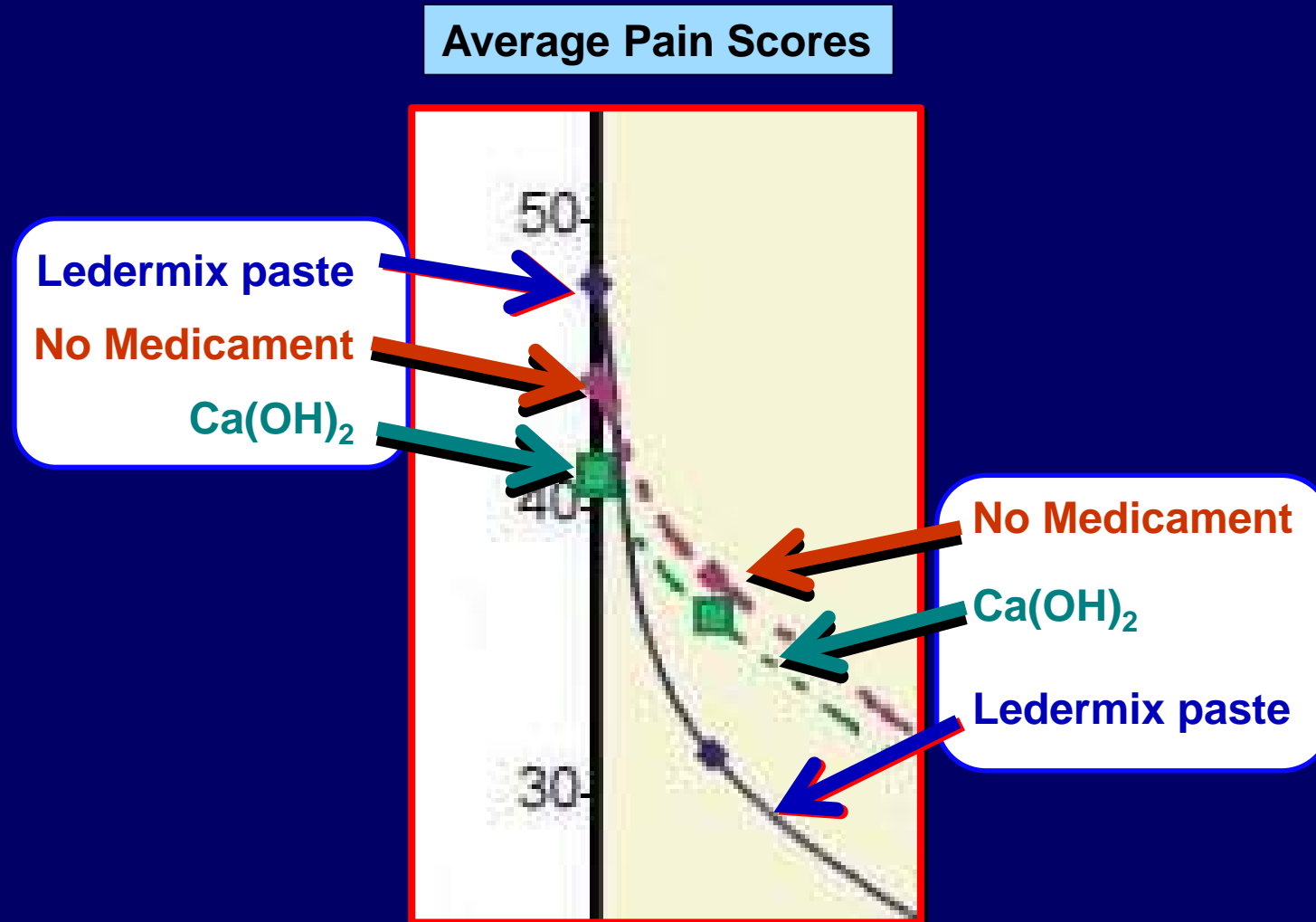
- ◆ **Ledermix group:** Significantly less post-operative pain than the Ca(OH)_2 group and the control group
 - Started with higher average pre-op. pain score
 - At the 4 hours post-operative interval:
 - The greatest effect was noted
 - Pain level was well below the other groups
 - Pain level remained well below the other medicaments for the next 4 days



Post-op Pain + Medicaments Ehrmann et al - IEJ 2003

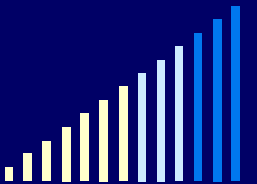
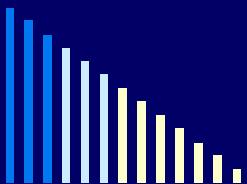


Post-op Pain + Medicaments Ehrmann et al - IEJ 2003



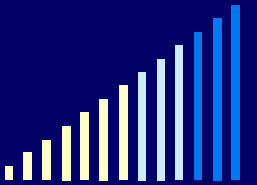
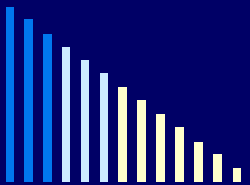
Post-op Pain + Medicaments Ehrmann *et al* - IEFJ 2003

- ◆ **CONCLUDED:** **Ledermix paste** is an effective intracanal medicament for the control of post-operative pain associated with acute apical periodontitis
- ◆ *“The rapidity of action of the medicament with corticosteroid was striking”*



Why Use Medicaments ?

- ◆ Anti-bacterial action
 - Residual bacteria in canals, tubules, fins, etc
 - Contaminants between visits
 - Periapical region
 - Periodontal tissues
- ◆ Reduce periapical inflammation
- ◆ Prevent or reduce pain
- ◆ Stimulate periapical repair
- ◆ **Prevent or inhibit inflammatory resorption**



The effect of an antibiotic/corticosteroid paste on inflammatory root resorption *in vivo*

Pierce A, Lindskog S.

OS : OM : OP 1987; 64: 216-20.



RESULTS (% of root surface)

No Medic^m

◆ Normal PDL	0		
◆ Inflammation in PDL	8.0		
◆ Surface resorption	0	+	= 97.3 %
◆ Inflammatory resorption	89.3		
◆ Ankylosis (replacement res ⁿ)	2.7		

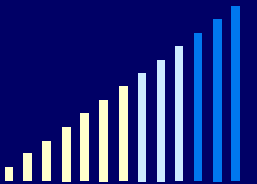
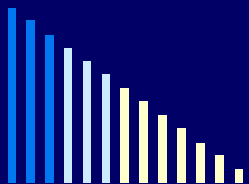
CS-Ab Paste & Inflammatory Resorption

Pierce & Lindskog OS:OM:OP 1987

RESULTS (% of root surface)

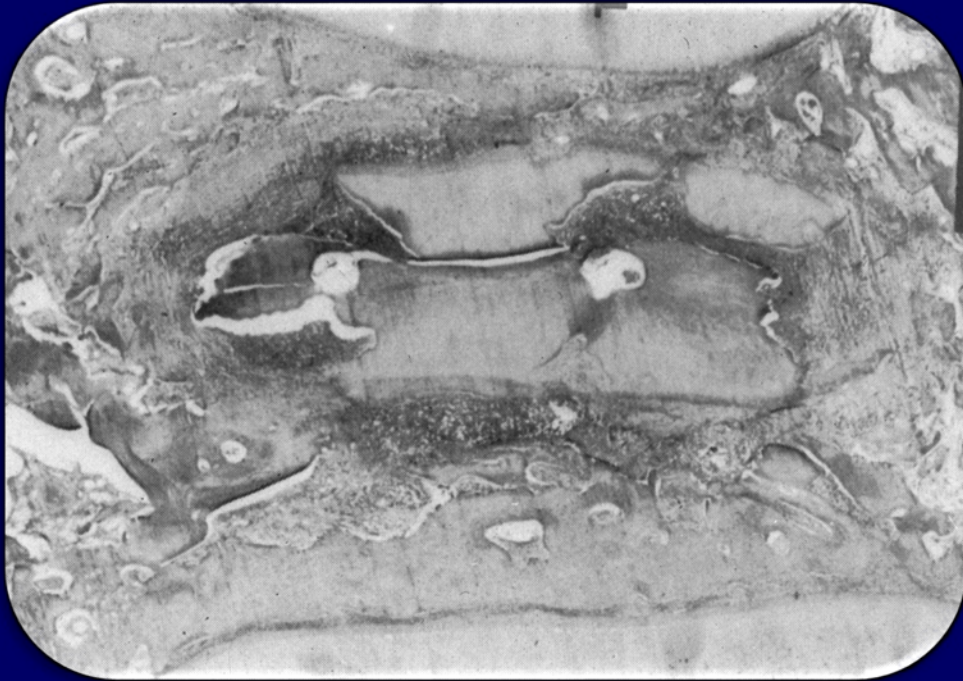
	No Medic ^m	Ledermix
◆ Normal PDL	0	6.9
◆ Inflammation in PDL	8.0	0
◆ Surface resorption	0	25.1
◆ Inflammatory resorption	89.3	0
◆ Ankylosis (replacement res ⁿ)	2.7	68.0

Bench-dried for 1 hour before replanting

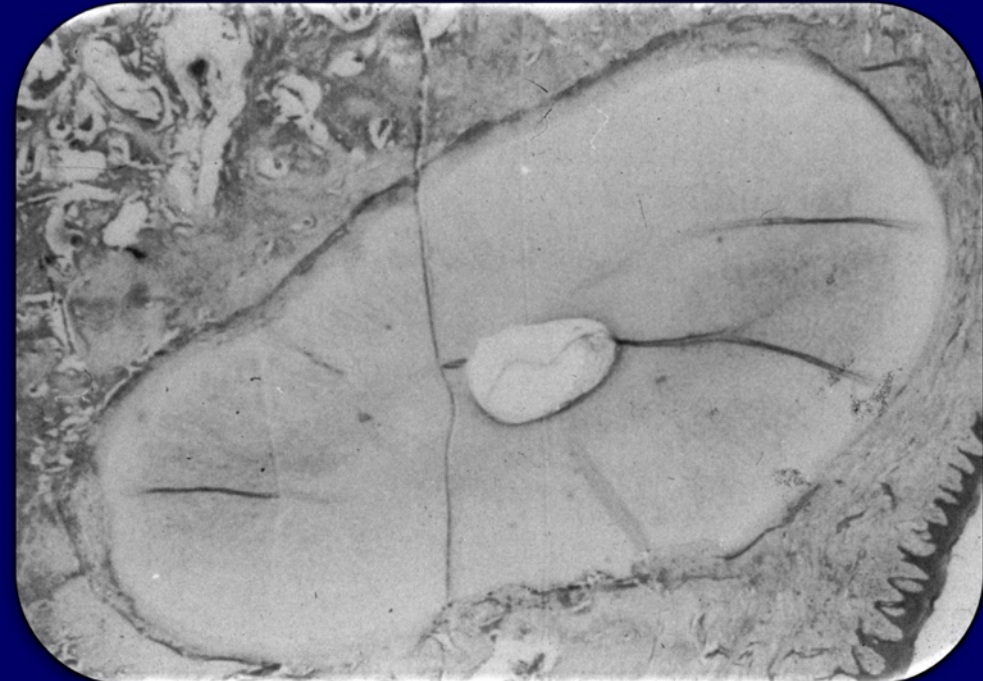


CS-Ab Paste & Inflammatory Resorption

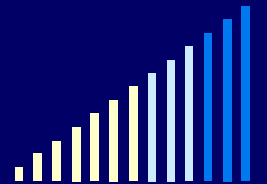
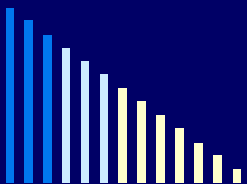
Pierce & Lindskog OS:OM:OP 1987



No Medicament



Ledermix paste



Evidence for direct inhibition of dentinoclasts by a corticosteroid / antibiotic endodontic paste

Pierce A, Heithersay G, Lindskog S.

Endod Dent Traumatol 1988; 4: 44-5



Direct inhibition of dentinoclasts by a CS-Ab paste

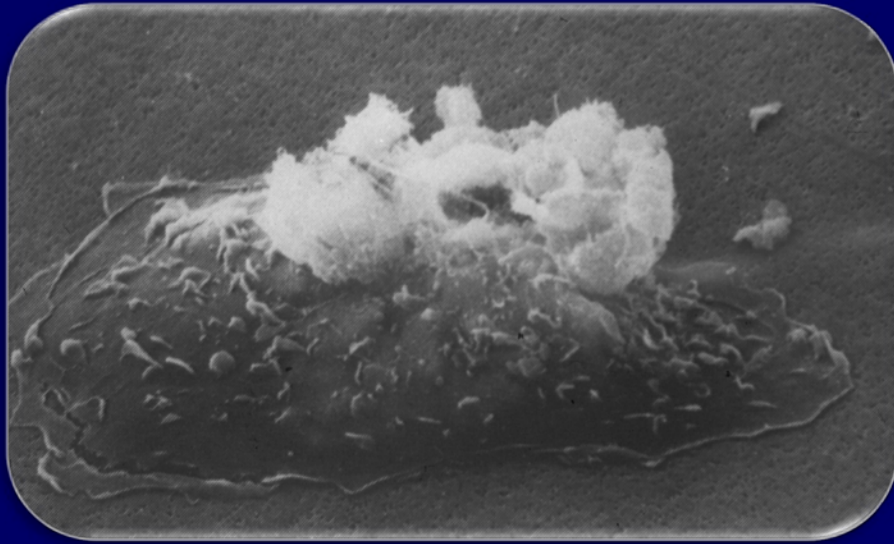
Pierce *et al* EDT 1988; 4: 44-5

- ◆ Dentinoclasts isolated from rat teeth undergoing inflammatory root resorption
- ◆ Exposed to:
 - Demeclocycline, or
 - Ledermix paste



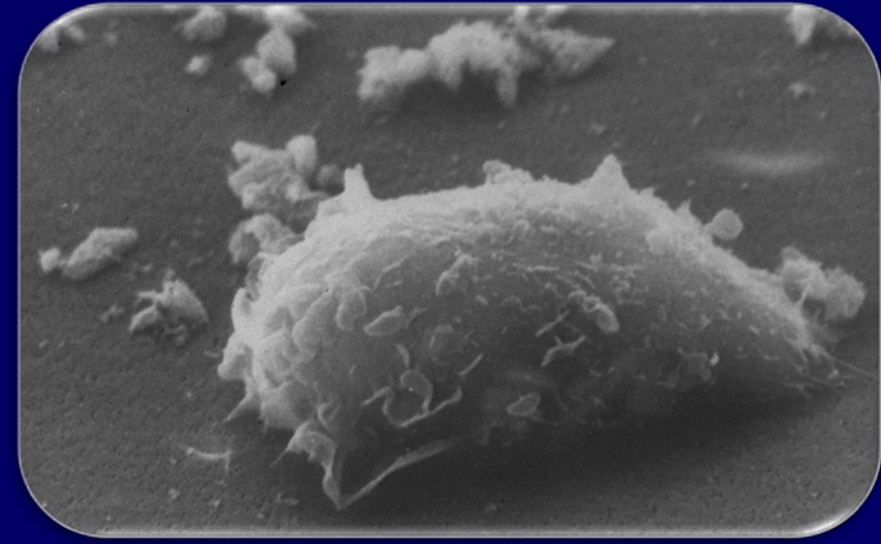
Direct inhibition of dentinoclasts by a CS-Ab paste

Pierce *et al* EDT 1988; 4: 44-5



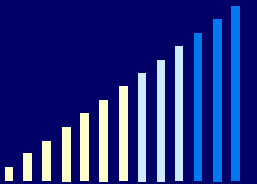
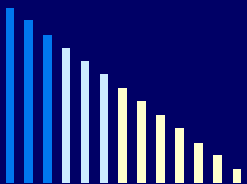
◆ Demeclocycline

- Cells well-spread
- Still attached after 24 hrs



◆ Ledermix paste

- Cells not spreading
- More spherical shaped
- No dentinoclasts evident after 18 hours



Direct inhibition of dentinoclasts by a CS-Ab paste

Pierce *et al* EDT 1988; 4: 44-5

- ◆ Results suggest that the steroid component of Ledermix paste has a direct inhibitory effect on resorbing cells
 - **Consistent with the effects of steroids on osteoclasts**
→ Suda *et al* 1983
- ◆ The antibiotic component also contributes to the therapeutic effect on inflammatory resorption by eliminating bacteria from the canal and from the tubules

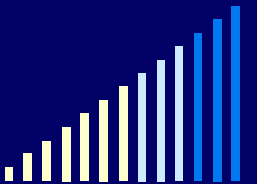
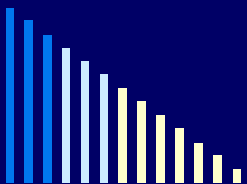


Non-antimicrobial properties of tetracyclines

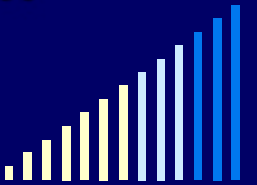
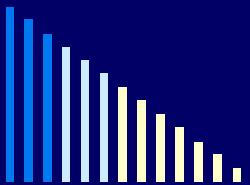
Vernillo et al - Curr Opin Perio 1994; 2: 111-8

Tetracyclines modulate host responses

- ◆ Inhibit osteoclast function
 - Synthetic tetracyclines are more potent than tetracycline
- ❖ Bind to bone and teeth
 - Slows release, prolongs action



- ◆ **Consistent with animal studies using TETRACYCLINES**
 - **Sae-Lim *et al* 1998**
 - Inflammatory resorption model in dogs
 - Tetracycline better than amoxicillin and control (no AB)
 - **Sae-Lim *et al* 1998**
 - Replacement resorption model in dogs
 - Tetracycline better than amoxicillin and control (no AB)
 - **Cvek *et al* 1990**
 - Topical doxycycline on replanted monkey teeth
 - Tetracycline reduced ankylosis, replacement resorption and inflammatory resorption



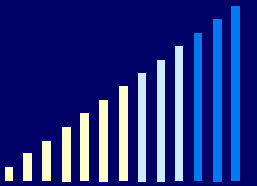
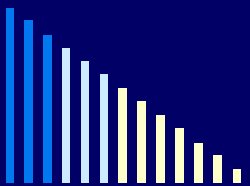
◆ Consistent with animal studies using CORTICOSTEROIDS

■ Sae-Lim *et al* 1998

- Replacement resorption model in dogs
- Topical dexamethasone better than systemic dexamethasone and control (Viaspan)

■ Chen *et al* 2005

- Replacement and Inflammatory resorption model in dogs
- Immediate endodontic treatment
- Triamcinolone alone better than tetracycline alone
- Ledermix paste better overall



Effect of immediate intracanal placement of Ledermix paste on healing of replanted dog teeth after extended dry times

Bryson E, Levin L, Banchs F, Abbott P, Trope M.

Dent Traumatol 2002; 18: 316-21



Immediate Placement of Ledermix Paste -v- Ca(OH)_2

Bryson, Levin, Banchs, Abbott & Trope *Dent Traumatol* 2002

- ◆ Teeth extracted, left dry for 1 hour, replanted
- ◆ Canals cleaned and filled with:
 - Ledermix paste
 - or
 - Ca(OH)_2 paste
- ◆ Examined histologically after 4 months for:
 - Inflammatory & replacement resorption
 - Residual root mass



Immediate Placement of Ledermix Paste -v- Ca(OH)_2

Bryson, Levin, Banchs, Abbott & Trope *Dent Traumatol* 2002

	No Resorption	Infl ^m + Repl ^m Res ⁿ
Ledermix *	59 %	41 %
Ca(OH)_2	14 %	86 %

* Significant difference for all criteria



Immediate Placement of Ledermix Paste -v- Ca(OH)_2

Bryson, Levin, Banchs, Abbott & Trope *Dent Traumatol* 2002

	No Resorption	Infl ^m + Repl ^m Res ⁿ	Residual Root Mass
Ledermix *	59 %	41 %	81 %
Ca(OH)_2	14 %	86 %	13 %

* Significant difference for all criteria



Immediate Placement of Ledermix Paste -v- Ca(OH)_2

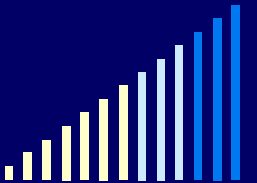
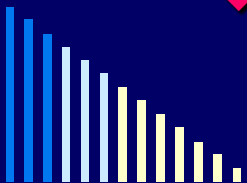
Bryson, Levin, Banchs, Abbott & Trope *Dent Traumatol* 2002

“Teeth immediately treated with Ledermix exhibited significantly more healing, less resorption and maintained more residual root mass than those treated with Ca(OH)_2 ”



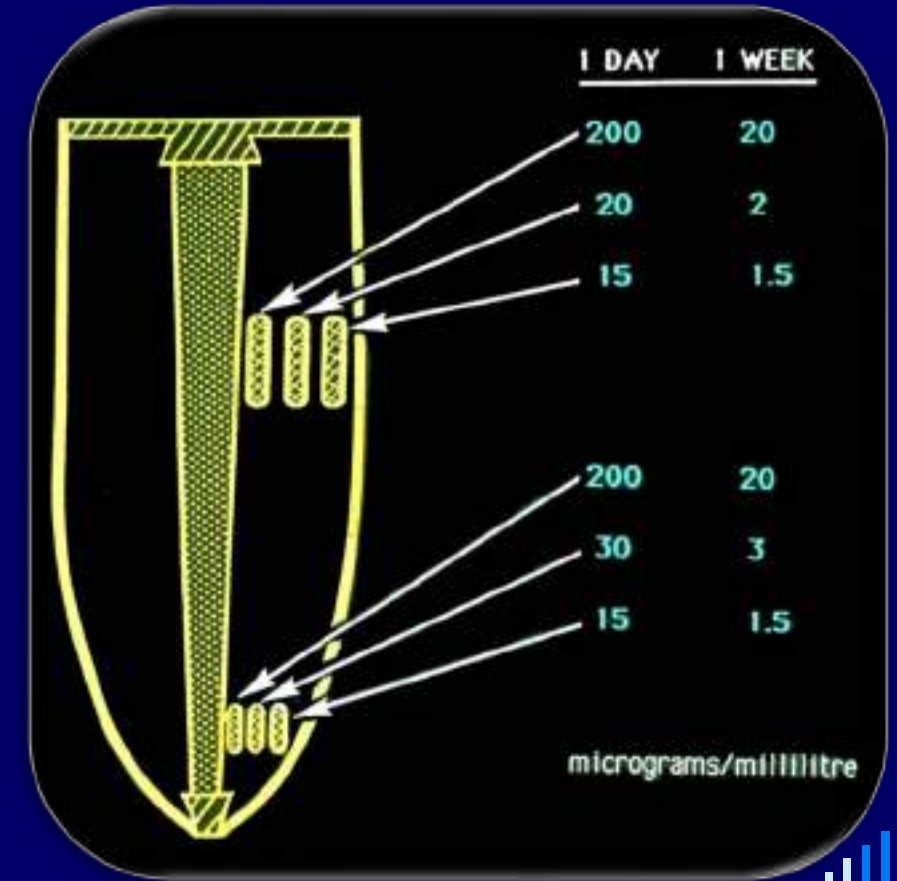
Why Use Medicaments ?

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 - Contaminants between visits
 - Periapical region
 - Periodontal tissues
- ◆ **Reduce periapical inflammation**
- ◆ **Prevent or reduce pain**
- ◆ **Stimulate periapical repair**
- ◆ **Prevent or inhibit inflammatory resorption**



Limitations of Ledermix Paste

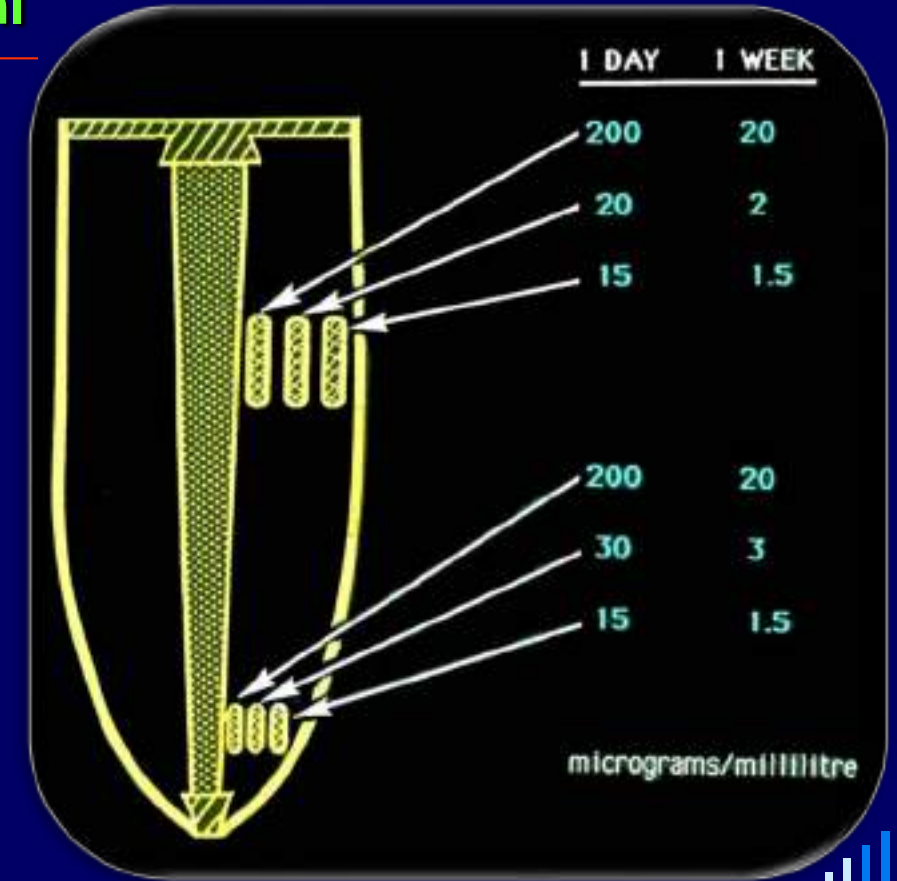
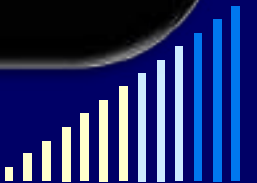
- ◆ **Anti-bacterial action is limited**
 - Compare AB concentrations in the dentine with the MIC₁₀₀ values for the commonly found bacteria in infected root canal systems



Ledermix paste - Diffusion Abbott et al EDT 1988, 1989

MIC₁₀₀ values for demeclocycline and common endodontic microbes

Organism	Micrograms / ml
<i>B. fragilis</i>	128
<i>B. oralis</i>	128
<i>B. melaninogenicus</i>	64
<i>Peptostreptococcus</i>	64
<i>Veillonella</i>	64
<i>Eubacterium</i>	64
<i>Propionibacterium</i>	32
<i>Lactobacillus</i>	32
<i>Streptococci</i> (aerobic)	32
<i>Actinomyces</i>	16
<i>Fusobacterium necrophorum</i>	16
<i>Fusobacterium nucleatum</i>	0.5

[illegible][illegible]

Limitations of Ledermix Paste

◆ Anti-bacterial action is limited

- Compare AB concentrations in the dentine with the MIC₁₀₀ values

- Within the canal

→ Excellent levels of AB

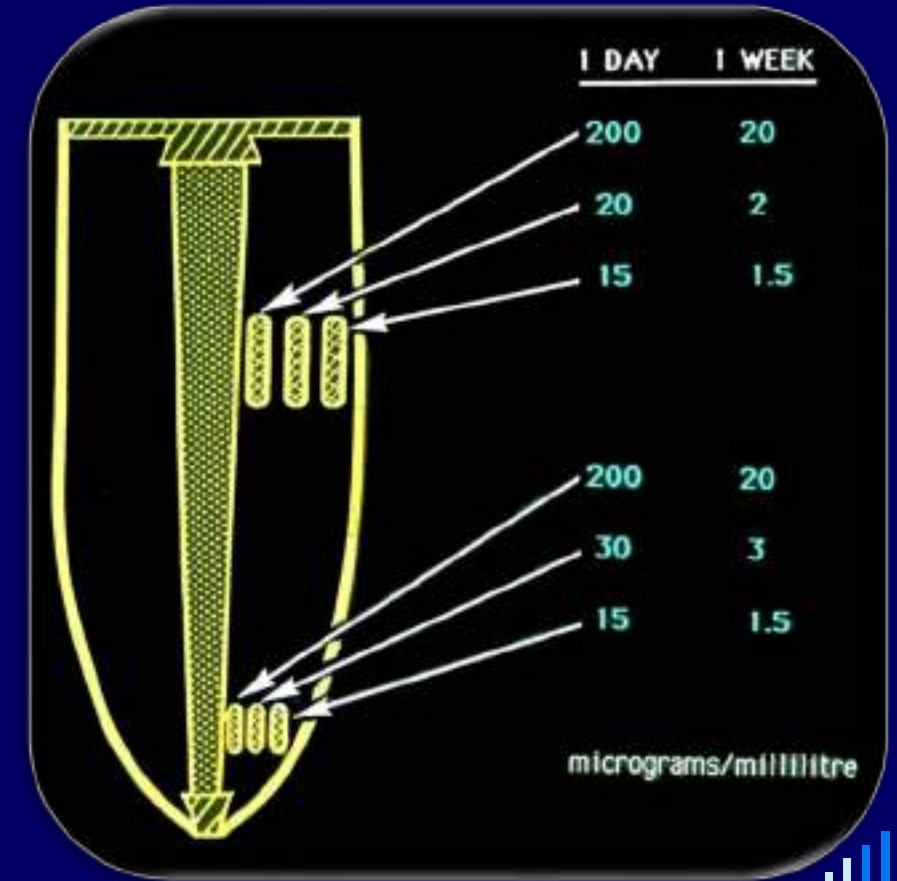
- Within dentine

→ Adjacent to canal: Reasonable

→ Periphery: Insufficient

- Within peri-radicular tissues

→ Insufficient to be predictable



The release and diffusion through human coronal dentine *in vitro* of triamcinolone and demeclocycline from Ledermix® paste

Johns P, Jones M, Williams G. The release and diffusion through human coronal dentine *in vitro* of triamcinolone and demeclocycline from Ledermix® paste. *Endothel* 1984; 1: 50-52.

Abstract: Coronal dentin from 10 human teeth was used as a model for the release and diffusion of triamcinolone and demeclocycline from Ledermix® paste. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell.

Introduction: Ledermix® paste is a combined antibiotic and steroid preparation used in the treatment of pulpitis and periapical inflammation. The paste contains triamcinolone and demeclocycline. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell.

Materials and Methods: Coronal dentin from 10 human teeth was used as a model for the release and diffusion of triamcinolone and demeclocycline from Ledermix® paste. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell.

Results: The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell.

Conclusions: The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell. The release and diffusion of triamcinolone and demeclocycline from Ledermix® paste was studied *in vitro* using a diffusion cell.

References: 1. Ledermix® paste. *Endothel* 1984; 1: 50-52. 2. Ledermix® paste. *Endothel* 1984; 1: 50-52. 3. Ledermix® paste. *Endothel* 1984; 1: 50-52.

Keywords: Ledermix® paste, triamcinolone, demeclocycline, diffusion, dentine.

Abbreviations: AB, antibiotic; MIC, minimum inhibitory concentration; MIC₁₀₀, minimum inhibitory concentration at 100% inhibition.

Correspondence: Dr. P. Johns, School of Dentistry, University of Liverpool, 6-10, Chester Road, Chester, CH2 3BP, UK.

Received: 10 October 1984; **Accepted:** 10 November 1984.

Limitations of Ledermix Paste

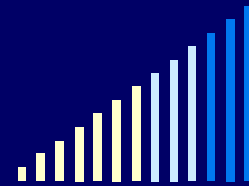
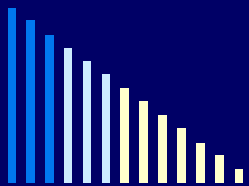
- ◆ Anti-bacterial action is limited
- ◆ Increasing order of anti-bacterial effectiveness:
 - Ledermix < Ledermix / Ca(OH)_2 < Ca(OH)_2

Athanassiadis, Abbott, George, Walsh

- *Aust Dent J* 2009, 2010, 2010



Endodontic Medicaments



Endodontic Medicaments

Abbott PV.

Australian Dental Journal

Literature Review → 1990; 35: 438-48

Guidelines for Clinical Use → 1990; 35: 491-6

Medicaments: Aids to success in endodontics. Part 1. A review of the literature

Paul V. Abbott, BDS(WA), MDS(Ad), FRACDS(Endo)*

Key words: Endodontics, medicaments.

Abstract

Bacteria play a major role in pulpal and periapical disease. They are capable of surviving in dentinal tubules and other canal ramifications that are inaccessible to mechanical instrumentation and irrigation. In order to predictably achieve bactericidal root canal systems, especially in rootless teeth, it is necessary to use intra-canal medicaments. These medicaments must be capable of destroying bacteria, reducing inflammation and stimulating hard tissue formation whilst not being toxic to the host tissues. Consideration of a material's therapeutic action must be made when selecting a medicament for any pathological condition. Many of the commercial preparations do not satisfy the requirements for the ideal root canal medicament.

(Received for publication March 1989. Revised December 1989. Accepted January 1990.)

Introduction

Endodontic treatment is most commonly performed on teeth because the pulp or the periapical tissues or both are either inflamed and/or infected. The most common cause of pulpal and periapical inflammation is infection. One of the primary goals of endodontic therapy must be to eliminate bacteria from the root canal system. This can be achieved by a combination of mechanical debridement and chemotherapy.

Based on a lecture presented at the Australian Dental Association 25th Congress, Sydney, 15-20 May 1988.
*Visiting Lecturer in Endodontics, The University of Western Australia, Visiting Consultant Endodontist, Perth Dental Hospital, Western Australia.

The role of bacteria

The role of bacteria in pulpal and periapical disease has been well researched in animals. Kakehaki and co-workers demonstrated in two studies^{1,2} that pulps which were exposed to the oral environment in germ-free rats were capable of healing whereas bacterially-contaminated pulps displayed degeneration. A recent series of reports³⁻⁶ (also on germ-free rat pulps) confirmed the ability of pulps to heal if there was no contamination from bacteria. In general, there was a lack of inflammation and dentine bridges formed. However in the coronaries and animals the responses included inflammation, pulp necrosis and lack of dentine bridge formation. Inflammation in the periapical tissues of rats has also been shown to be directly related to bacterial invasion of the root canal.⁷

In 1976, a comprehensive study of necrotic human dental pulps by Sundqvist⁸ demonstrated that all cases with a periapical radiolucent lesion had microbes in the root canal system and there were always between two and twelve strains of bacteria present. A correlation was shown to exist between the number of strains present and cases with acute periapical inflammation. In addition, patients with pain had more than six strains and those with large periapical lesions had more strains than cases with smaller lesions. These⁹ cases showed a correlation with the presence of a specific organism, *Escherichia coli*.

The role of bacteria in periapical disease was further demonstrated in monkeys by Miller et al.¹⁰ and Fabricius et al.¹¹ In these experiments teeth were aseptically devitalized by pulp amputation one to two millimeters from the apex with a Hedström file. Some teeth were immediately closed and others were left open to the oral cavity for seven days and then sealed. Histological analysis revealed that no

Australian Dental Journal 1990;35(5):438-48.



Medicaments: Aids to success in endodontics. Part 2. Clinical recommendations

Paul V. Abbott, BDS(WA), MDS(Ad), FRACDS(Endo)*

Key words: Endodontics, medicaments.

Abstract

In order to predictably achieve bactericidal root canal systems, especially in rootless teeth, it is necessary to use intra-canal medicaments. Medicaments can also be used to influence the peri-radicular response to endodontic treatment. Consideration of a material's therapeutic action must be made when selecting a medicament for any pathological condition. In general, only two commercial preparations satisfy the general requirements for root canal medicaments. Guidelines and the rationale for the use of these preparations are presented.

(Received for publication March 1989. Revised December 1989. Accepted January 1990.)

Introduction

In Part 1 of this review,¹ the role of bacteria in the progression of pulp and periapical diseases was discussed. The inter-apoptosis medication of root canals was shown to be a predictable means of eliminating bacteria from root canal systems and a reliable method for reducing periapical inflammation and stimulating hard tissue formation. However, some medicaments are capable of causing inflammation due to the toxicity of some components.

Based on a lecture presented at the Australian Dental Association 25th Congress, Sydney, 15-20 May 1988.
*Visiting Lecturer in Endodontics, The University of Western Australia, Visiting Consultant Endodontist, Perth Dental Hospital, Western Australia.

There are many commercial preparations marketed as endodontic medicaments. In choosing a medicament, the operator must be aware of the full list of the components and their respective concentrations and effects to the pulp and peri-radicular tissues. The decision should be based on an assessment of the risk versus benefit ratio and only a material that will produce a favourable response should be chosen.

Part 1¹ outlined the various advantages and disadvantages of the common commercial preparations and concluded that more than one medicament was required to achieve all of the aims of medicating canals. Two preparations satisfy the general requirements for medicaments, Ledermix¹ paste and Pulpdent² paste but they require sequential or combined use to achieve the full range of desired therapeutic responses.

The following is an outline of the clinical considerations for using medicaments and recommendations for medication regimens for pathological conditions that can be treated by conservative endodontic therapy.

Time of use of medicaments

In general, it takes 10-15 days for inflammation to subside or heal.³ The use of anti-inflammatory medicaments such as Ledermix paste can provide rapid relief of symptoms. However, the absence of symptoms does not indicate the lack of pathology. Therefore, consideration of total healing time is required prior to completing a root canal filling. Thus, the minimum inter-apoptosis time interval should be 10 days, unless symptoms are

Ledermix Pharmaceuticals, Wallendene, West Gwent, Dyfed, Gwent, Wales, NP23 5TA.

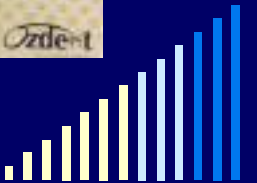
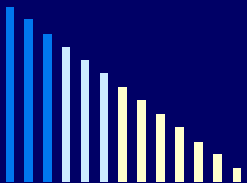
Australian Dental Journal 1990;35(5):491-6.

491

Endodontic Medicaments

Choices:

- ◆ Corticosteroid / antibiotic - CS / AB
 - e.g. **Ledermix paste**
- ◆ Calcium hydroxide - Ca(OH)_2
 - e.g. **Calasept Plus paste, Calmix**
- ◆ 50:50 mixture - CS / AB + Ca(OH)_2
 - e.g. **Ledermix + Calasept Plus pastes**



Endodontic Medicaments

Major Functions and Choices:

◆ Anti-inflammatory

➤ Ledermix paste

e.g. Irreversible Pulpitis

Acute Ap. Periodontitis



◆ Anti-bacterial

➤ Ledermix paste

e.g. RCF + infected RCS

Pulpless, infected RCS

➤ Calcium hydroxide - Ca(OH)_2



◆ Stimulate hard tissue repair

➤ Calcium hydroxide - Ca(OH)_2

e.g. Apexification



50:50 mix of Ledermix / Ca(OH)_2

- ◆ Originally used by Schroeder - 1962, 1972, 1981
- ◆ Advocated by Heithersay - 1984, 1986
- ◆ Promoted by Abbott - 1990, 1999



Bar chart showing the number of people in the population aged 15 and over, by sex and age group, for the years 2000, 2005, and 2010. The chart shows a general decline in population across all age groups and sexes, with a more pronounced decline for males than females.

-
- | Age Group | Number of People (Millions) |
|-----------|-----------------------------|
| 0-4 | ~0.5 |
| 5-9 | ~0.6 |
| 10-14 | ~0.7 |
| 15-19 | ~0.8 |
| 20-24 | ~0.9 |
| 25-29 | ~1.0 |
| 30-34 | ~1.1 |
| 35-39 | ~1.2 |
| 40-44 | ~1.3 |
| 45-49 | ~1.4 |
| 50-54 | ~1.5 |
| 55-59 | ~1.6 |
| 60-64 | ~1.7 |
| 65-69 | ~1.8 |
| 70-74 | ~1.9 |
| 75+ | ~2.0 |

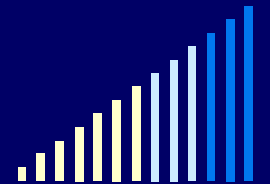
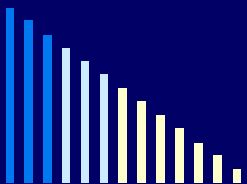
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250

10

50:50 mix of Ledermix / $\text{Ca}(\text{OH})_2$

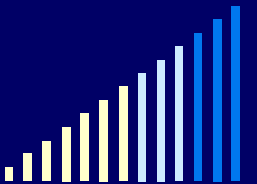
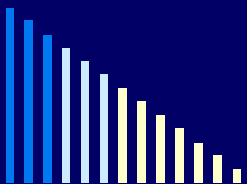
- ◆ Slower release of Ledermix paste components
 - Dressing lasts longer than Ledermix paste used alone
 - Maintains canal sterility for longer
- ◆ No change in activity of components
- ◆ Increased anti-bacterial spectrum compared to Ledermix paste used alone
- ◆ Only a small reduction in pH levels reached in dentine
- ◆ Lower tissue toxicity
 - Compared with $\text{Ca}(\text{OH})_2$



50:50 mix of Ledermix / Ca(OH)_2

◆ 50:50 mix of CS / AB & Ca(OH)_2

- Saline-based Ca(OH)_2 - e.g. Calasept Plus
 - Pre-mix on a glass slab
 - Then apply the mixture with a file or spiral filler
- Methyl cellulose based / PEG Ca(OH)_2 - e.g. Pulpdent, Calmix
 - Place the CS / AB in the canal first (with file or spiral filler)
 - Then place the Ca(OH)_2 in canal - i.e. mix in the canal (with file or spiral filler)



My Typical Treatment Approach

1st Appointment

- ◆ Consult & Diagnose
- ◆ Investigate
- ◆ Negotiate Canals
- ◆ Medicate canals
- ◆ Interim Restoration

4-6 wks

2nd Appointment

- ◆ Working Lengths
- ◆ Prepare Canals
- ◆ Re-medicate canals

4-6 wks

3rd Appointment

- ◆ Root Canal Filling
- ◆ Refer back to Dentist

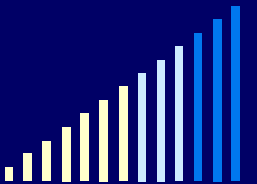
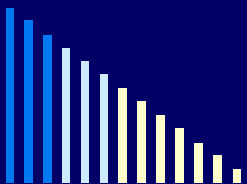
Medicaments

Irreversible Pulpitis or Elective RCT -

1. Ledermix Paste
2. Ledermix + $\text{Ca}(\text{OH})_2$

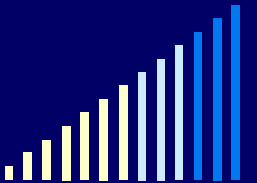
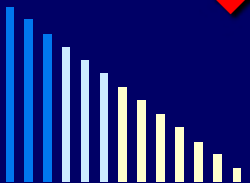
Infected Canals and Apical Periodontitis -

1. Ledermix + $\text{Ca}(\text{OH})_2$
2. $\text{Ca}(\text{OH})_2$



Summary

- ◆ The Ledermix materials have been used extremely successfully for almost 60 years
- ◆ Significant scientific research supports their use
 - ➔ Clinical, radiographic, histological, humans, animals, etc
- ◆ Major function: Anti-inflammatory
- ◆ Second function: Anti-resorption
- ◆ Third function: Anti-bacterial
- ◆ There are many mis-conceptions / perceptions
 - ➔ It's time for the “anti” people to move on !!!

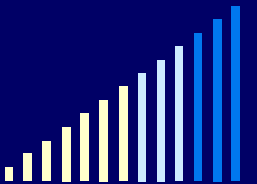
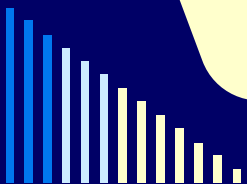


The Ledermix Story

◆ Some of the concerns were:

- Systemic side effects of steroids
 - Inability of steroids to stimulate bone growth
 - Steroids lead to chronic osteomyelitis and bone necrosis
 - Development of resistance in organisms
 - Development of alternative agents to tetracyclines
- agents may be available

**NONE of these concerns were valid in the 1960's
..... and they are still NOT valid today !!!**



The Ledermix Materials - Fact or Fiction?

Scientifically-based Indications for Their Use in Everyday Dentistry



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**Thank
you**

