Ledermix Cement:
The Myths and the (Scientific) Facts

Hosted by: Professor Paul V. Abbott AO

BDSc, MDS, FRACDS(Endo), FPFA, FADI, FICD, FACD, FIADT
Specialist Endodontist
Winthrop Professor of Clinical Dentistry
School of Dentistry
The University of Western Australia
Ledermix Cement
The Myths and the (Scientific) Facts

NOTE: Ledermix Paste – will NOT be discussed in this lecture

Background Information

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

- **Ledermix Cement**
  - Developed in 1962
Prof. André Schroeder

1918 - 2004 (86 yrs old)

Significant Contributions

- 1952: AH26 cement
- 1960: Ledermix Paste
- 1962: Ledermix Cement
- 1976: ITI Implant system

University of Bern, Switzerland

- 1959-84: Professor and Chair - Dept. of Operative Dentistry
- 1971-73: Dean - Medical Faculty
- 1979-80: President - University of Bern
Some History...

- Corticosteroids first used in Dentistry to treat **TMJ problems** (Spies et al. 1952, Strean 1952)
- Hydrocortisone injected into the TMJ (Horton 1953)
- 1954 - Henny stated:
  - “The specific action of the steroid is solely directed against inflammation”
  - “Permanent success can only be expected if, at the same time, the causative factor (i.e. traumatic occlusion) is removed”

Some History...

- Corticosteroids were also used to treat periodontal and mucosal disorders (Siegmund 1952)
- Topical or systemic hydrocortisone for gingivitis with or without mechanical cleaning (Fisher 1956)
  - Reduced inflammation which was enhanced if mechanical cleaning also
- Topical corticosteroids used for gingivitis, leukoplakia, pemphigus, herpes, aphthous ulcers (Weisstein 1956)
Corticosteroids were first used in *Endodontics* to treat **acute apical periodontitis** by flushing the canal with hydrocortisone
- “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)

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1962 - Schroeder emphasised:
- “Treatment with corticosteroids is not a causal therapy but is merely adjunctive and therefore the causative factor must be removed by conventional means”
- “Acute inflammation responded far more successfully than chronic inflammation”
- “Prednisolone allowed shorter period of treatment than hydrocortisone”
Some History...

- Clinical and histological studies done:

- Initially used hydrocortisone

- Then used triamcinolone
  - A more potent corticosteroid

- Combined with: chloramphenicol and xylocaine
  - In an ointment base

Some History...

- Procedure (Schroeder 1960):
  - 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
Some History…

- 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)

Some History…

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

- 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 combined:
  - CS - anti-inflammatory
  + AB - antibacterial
  + Ca(OH)$_2$ - dentinogenic and anti-bacterial
  + ZO-E - anti-inflammatory and anti-bacterial

Some History…

- Schroeder further stated that the CS has two main goals:
  1. Prevent acute exacerbation of already inflamed tissues
  2. Prevent the necrosis caused by Ca(OH)$_2$

- And the ZO-E does not affect the Ca(OH)$_2$
  - Whereas Zn$_3$(PO$_4$)$_2$ is acidic and may neutralise the Ca(OH)$_2$ making it less effective
Some History...

- So … Schroeder then mixed equal volumes of Ledermix paste with Ca(OH)$_2$ powder and applied it 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

Some History...

- So … Schroeder then mixed equal volumes of Ledermix paste with Ca(OH)$_2$ powder and applied it as a pulp cap

- Excellent results were reported !!!
  - Rapid pain relief
  - Pulps had survived when reviewed
    - With pulp tests, radiographs, etc.
Some History...

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

Schroeder 1981

In Humans

In Humans and in Monkeys

Schroeder 1981
Some History…

- 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 the desired therapeutic aims with one material
  - Have a hard setting compound - ease of use
    - can restore immediately

Hence: Ledermix Cement was manufactured
Ledermix Cement Schroeder (1962)

- **CS**: Triamcinolone - 0.67 %
- **AB**: Demeclocycline - 2.0 %
- Calcium hydroxide - 33.4 %
- Zinc oxide - 47.2 %

+ Eugenol - 85% of the liquid

Forms a hard-setting cement when mixed

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Some History...

- **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 to tetracyclines
  - More specific anti-microbial agents may be available
Some History…

- Often claimed that Ledermix is “banned in the USA”
  - I still OFTEN hear this today!!!

- This is “FAKE NEWS” !!!!
  - It has NEVER been banned

- But it is also VERY OLD “NEWS” !!!!!

Some History…

- 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 very small market
      - Despite me trying to persuade them!!
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

- 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
Ledermix Cement

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

Table 1. Summary of corticosteroid details

<table>
<thead>
<tr>
<th>Corticosteroid &amp; Potency</th>
<th>Maximum amount of Ledermix used in tooth (mg)</th>
<th>Maximum amount of triamcinolone in tooth (mg) (Cortisol equivalent)</th>
<th>Triamcinolone released after 1 day (mg) (Cortisol equivalent)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exogenous cortisol in humans</td>
<td>&lt; 100 mg/day</td>
<td>0.37 (1.85)</td>
<td>0.26 (1.3)</td>
</tr>
<tr>
<td>Cortisol in ‘stress situations’</td>
<td>20–30 mg/day</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cortisol triamcinolone potency</td>
<td>1:5</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Ledermix Cement

? Inability of steroids to stimulate calcific repair

- Mixed reports from histological studies
  - Schroeder 1981

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

? Inability of steroids to stimulate calcific repair

- Mixed reports
- BUT - the

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

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Ledermix Cement

- 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
  - A 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 !!

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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

Steroids lead to chronic inflammation and/or pulp necrosis

- NOT supported by clinical and histological studies
  - Schroeder 1981
  - And many others
Ledermix Cement

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

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

Ledermix Cement

How does it work in teeth?
- Actions are based on the therapeutic properties of each component
  - CS: Triamcinolone - 0.67%
  - AB: Demeclocycline - 2.0%
  - Ca(OH)₂ - 33.4%
  - Zinc oxide - 47.2%
  - Eugenol - 85% of the liquid
Ledermix Cement

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- Triamcinolone
  - Anti-inflammatory agent

- Calcium hydroxide
  - Promotes dentine repair

- Zinc oxide - Eugenol
  - Anti-inflammatory and anti-bacterial

Not necessary to include - sufficient anti-bacterial action from the Ca(OH)$_2$ and the Eugenol

Ledermix Cement

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

- Triamcinolone
  - Anti-inflammatory agent
    - \textit{In vitro} - 70\% is released by the end of day 1
    - Rest by the end of day 3 (Hume & Kenney - JoE 1981)

- Calcium hydroxide - 33.4 \%
- Zinc oxide-eugenol - 47.2 \%

- Expect this to be much faster when \textit{In Vivo}
  - \textit{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
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
  - Anti-inflammatory agent (1-3 days maximum effect)
- Calcium hydroxide
  - Promotes dentine repair (numerous studies)
- Zinc oxide - Eugenol
  - Anti-inflammatory and anti-bacterial
**Calcium Hydroxide**

- Hard setting cements - e.g. Dycal, Life, etc
- Used for many years - since ~ 1920
- Long history with good healing rates
- Considerable research
  - Histological, clinical, radiographic, animals, humans, *in vivo, in vitro*, etc.
- Consistent findings & results

**Typical healing response with Ca(OH)$_2$**

*(Clarke 1970)*

- DEBRIS
- NECROSIS
- LYSED BLOOD
- DENSE ZONE
- CALCIFICATION
- PULP
Typical healing response with Ca(OH)$_2$

(Cvek 1989)

- Necrosis
- Calcified tissue
- Dentine bridge

Typical healing response with Ca(OH)$_2$

(Schroeder 1981)

- Necrosis
- Calcified tissue
- Dentine bridge
- Typical healing response with Ca(OH)$_2$ (Schroeder 1981)

- Necrosis
- Calcified tissue
- Dentine bridge

- Dentine “bridge” forms below the exposure site
- The necrotic layer manifests as a “hole” if the tooth is re-entered later
Typical healing response with Ca(OH)$_2$
(Schroeder 1981)

- NOT ALL cases form a dentine “bridge”
- Chronic inflammation may persist

Human Pulp Reactions to a Glucocorticosteroid-Antibiotic Compound

Healing responses - **Ledermix Cement**

**Robertson 1977**

- **Clinically Normal Pulp (Ortho. Extraction)**
  - NO inflammation, no “bridge”, no diffuse calcifications after Ledermix Cement pulpotomy

- **Reversible Pulpitis due to Caries**
  - NO inflammation, partial “bridge”, diffuse calcifications in root canal after Ledermix Cement pulpotomy

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**Ledermix Cement**

- **Triamcinolone** - 0.67 %
  - Anti-inflammatory agent (1-3 days maximum effect)

- **Calcium hydroxide** - 33.4 %
  - Promotes dentine repair (numerous studies)

- **Zinc oxide - Eugenol** - 47.2 %
  - Anti-inflammatory and anti-bacterial

Brännström et al. J Prosthet Dent 1979

Brännström’s “upside down restorations”

- Human teeth *in vivo*
- Class V cavities
  - Restored
  - Teeth extracted
  - Examined histologically
Brännström et al. *J Prosthet Dent* 1979

- Human teeth *in vivo*
- Class V cavities

- **Silicate restorations**
  - No lining
  - ? Acid effect on pulp

Silicate

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Brännström et al. *J Prosthet Dent* 1979

- Human teeth *in vivo*
- Class V cavities

- **Silicate restorations**
  - No lining
  - ? Acid effect on pulp

- **Silicate alone**
  - Pulp inflamed
  - Bacteria under restoration & in the tubules

Silicate
Human teeth *in vivo*

Class V cavities

Silicate restorations
  - No lining
  ? Acid effect on pulp

Silicate alone
  - Pulp inflamed
  - Bacteria under restoration & in the tubules

**✓** ZO-E cover
  - No pulp inflammation
  - No bacteria seen

*Brännström et al J Prosthet Dent 1979*

*Brännström’s “upside down restorations”*

**→** ZO-E prevented entry of bacteria into the cavities
**Zinc Oxide-Eugenol**

- **Zinc oxide - Eugenol**
  - Indirect pulp caps
  - 1 year later
  - No inflammation
  - Normal dentine formation
  
  *(Schroeder 1981)*

**Eugenol is released by progressive hydrolysis**

- **Hydrolysis occurs at**:
  - External surface (saliva)
  - Cavity floor (dentinal fluid)

ZOE  Diffusion

*(Hume '84, '86, '87)*
Ledermix Cement

- Triamcinolone
  - Anti-inflammatory agent (1-3 days maximum effect)
- Calcium hydroxide
  - Promotes dentine repair (numerous studies)
- Zinc oxide - Eugenol
  - Anti-inflammatory and anti-bacterial

Ledermix Cement

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

- Triamcinolone (CS)
- ZO-Eugenol
- Demeclocycline (AB)
- Ca(OH)₂
Ledermix Cement - Indications for Use

- Reversible Pulpitis (requires correct diagnosis !!!)
  - Deciduous and Permanent Teeth
    - Indirect Pulp Cap
    - Direct Pulp Cap
    - Pulpotomy - partial or full

- Asymptomatic teeth
  - Lining - when deep caries
    - To reduce inflammation that may be present due to the caries
    - To reduce inflammation from the operative procedures

- Temporary cement for provisional / temporary crowns following crown preparation
  - To reduce inflammation from the operative procedures

- Root canal filling material
  - Deciduous teeth
    - Irreversible pulpitis
    - Infected root canal system
      - Will resorb at a similar rate to the tooth roots
Ledermix Cement

Some Clinical Case Examples

Ledermix Cement - Indirect Pulp Cap

- Chronic Reversible Pulpitis - unsatisfactory restoration
- Symptoms resolved immediately
- Pulp tests normal at reviews: 3, 12 and 18 months
- Extracted after 18 months for Orthodontic reasons

Tooth 15

Female 26 yrs

Pre-operative

CO₂: +
EPT: 38

67

68
Ledermix Cement - Direct Pulp Cap

- Chronic Reversible Pulpitis - due to caries and unsatisfactory restoration
- Symptoms resolved immediately
- Pulp tests normal at reviews: 3, 12 and 24 months

 Tooth 37

Pre-operative | 2 years Recall

Female 47 yrs

Incorrect diagnosis / treatment by referring dentist
- No post-operative symptoms
- Pulp tests normal at reviews at 3 and 12 months + pulp canal calcification

 Tooth 42

Female 9 yrs

Ledermix Cement

Pre-operative | 6 months | 18 months

CO₂: ++ EPT: 25
CO₂: + EPT: 32
CO₂: + EPT: 25
CO₂: ? EPT: 33
CO₂: - EPT: 38
Female 10 yrs

Ledermix Cement - Partial Pulpotomy

- Complicated crown fracture - due to trauma
- No post-operative symptoms
- Pulp tests normal at reviews: 1, 12, 24 & 36 months + further root development

Tooth 11

CO₂: +
EPT: 22

1 month

CO₂: +
EPT: 24

12 months

CO₂: +
EPT: 21

2 years

CO₂: +
EPT: 25

3 years

71

Male 11 yrs

Ledermix Cement - Partial Pulpotomy

- Complicated crown fracture - due to trauma
- No post-operative symptoms
- Pulp tests normal at reviews: 3, 9 and 18 months + further root development

Tooth 11

CO₂: +
EPT: 30

3 months

CO₂: +
EPT: 29

18 months

72
Ledermix Cement - Cervical Pulpotomy

- Complicated crown fracture - due to trauma
- No post-operative symptoms
- Pulp tests normal at reviews: 6 months + further root development

**Tooth 13**

- Female
- 14 yrs
- Tooth 13
- Pre-operative
- 6 months

Ledermix Cement - Pulpotomy

- Acute Reversible Pulpitis - due to caries
- Symptoms resolved immediately
- Pulp tests normal at reviews at 3 and 12 months + further root development

**Tooth 36**

- Male
- 8 yrs
- Tooth 36
- Pre-operative
- Post-operative
- 1 year
Predictable Management of Cracked Teeth with Reversible Pulpitis

Abbott PV, Leow N.


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**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%

100%
**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%)

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**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 calcific repair
  - Steroids lead to chronic inflammation and/or pulp necrosis
  - Development of tetracycline-resistant microorganisms
  - Development of hypersensitivity reactions to tetracyclines
  - More specific antimicrobial agents may be available

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

Ledermix Cement

The Myths and the (Scientific) Facts

![Ledermix Cement Bottles]
QUESTIONS

Statements of attendance and webinar slides will be emailed shortly.