

# Is there life after Buckley's formocresol? Part II – Development of a protocol for the management of extensive caries in the primary molar

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**Summary.** *Objective.* To produce a working clinical protocol for pulp therapy techniques in the extensively carious primary molar.

*Introduction.* The International Agency for Research on Cancer has recently classified formaldehyde as carcinogenic to human beings. As such, a medicament that can be used to replace formocresol in clinical practice should be identified.

*Methods.* Part I of this paper explored the currently available alternative interventions and materials to formocresol in the form of a narrative review following an extensive literature search. Part II now presents the formation of a specialist group to establish an evidence-based protocol, for the management of the extensively carious primary molar.

*Conclusion.* A protocol and key points document have been developed to assist clinicians in their treatment planning. Areas for further postgraduate training are identified.

## Introduction

Buckley's formocresol was first introduced as a pulp medicament in 1904 [1], and since 1930 [2], it has been the treatment of choice for primary molar vital pulpotomies. There is much published work relating to its clinical use, with clinical success ranging from 55% to 98% [3–8]. Several studies in the 1970s demonstrated that a one-fifth dilution of formocresol was as effective as a full-strength solution in terms of its initial cytotoxicity to fibroblasts [9–12]. Concern over the use of formaldehyde has been voiced for some time [13, cited in 17, 14–17], but until recently, the evidence has been equivocal.

## Animal studies

Formaldehyde has been shown to be mutagenic in *Escherichia coli* bacteria [18,19] and the fruit fly *Drosophila* [20]. When administered in drinking water, formaldehyde produced an increase in total

malignant tumours in rats [21], and when inhaled, it has been shown to induce squamous cell carcinoma of the nasal cavity [22]. Long-term studies using rabbits have demonstrated that prolonged contact with formaldehyde may produce precancerous and cancerous states in the epithelium [23]. Other authors have suggested caution in extrapolating the findings of animal studies to human beings. In particular, the rat has been shown to be more susceptible to changes induced by inhaled formaldehyde [24].

## Human in vitro studies

Mammalian cell *in vitro* studies have demonstrated unscheduled DNA synthesis in HeLa cells as a result of formaldehyde application [25], and increased cell proliferation in respiratory mucosa [22]. Forward mutations have also been produced by formaldehyde in a human lymphoblastoid cell line [26]. Experimental evidence has suggested that inhaled formaldehyde vapour can exert toxic effects at remote sites as well as in the respiratory tract. Chromosomal aberrations [27,28], increased micronuclei [27,29,30], DNA–protein cross-links [31,32] and sister chromatid

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exchanges [27,32–34] have been found in peripheral lymphocytes of humans exposed to formaldehyde. Although there is an established link between chromosomal aberrations and cancer [35], the relationships between micronuclei or sister chromatid exchanges and health risks are less clear [36].

#### *Human cohort studies*

Long-term cohort studies of industrial workers have found increased risks for leukaemia, particularly myeloid leukaemia, in medical workers and other professionals exposed to formaldehyde [37,38], whilst other research does not support these findings [39]. Possible associations have also been suggested between occupational formaldehyde and cancer of the lung [39,40], nasopharynx [39,41], stomach [39], paranasal sinuses [42,43], prostate [41,44], brain [44] and pancreas [45]. However, these associations remain inconsistent.

#### *Dental studies*

Systemic distribution of radio-isotope-labelled formaldehyde has been demonstrated following formocresol pulpotomy in dogs [46] and rhesus monkeys [47]. Labelled formaldehyde has been found in periodontal ligament, bone, dentine and urine, and smaller amounts in the liver, kidney, lungs, skeletal muscle and cerebrospinal fluid within minutes of the pulpotomy [46]. More recently, a human case control study demonstrated a single case of mutagenicity in peripheral blood lymphocyte cultures following formocresol pulpotomy [48]. A correlation between formocresol pulpotomies in primary teeth and enamel defects in the permanent successor has been suggested [49], although other workers found no such links [50].

In June 2004, the International Agency for Research on Cancer (IARC) classified formaldehyde as carcinogenic to human beings [51]. The expert working group determined that there is now sufficient evidence that formaldehyde causes nasopharyngeal cancer in humans, limited evidence for cancer of the nasal cavity and paranasal sinuses, and strong but not sufficient evidence for a causal association between leukaemia and occupational exposure to formaldehyde. The IARC working group recommended further research in order to identify a mechanism for the induction of leukaemia and to build on the existing evidence base.

#### *Care pathways, clinical protocols and decision trees*

The National Pathway Association was founded in 1994 to support the development of integrated care pathways. A care pathway determines locally agreed, multidisciplinary practice based on guidelines and evidence, where available, for a specific patient group. It forms all, or part of, the clinical record, documents the care given and facilitates the evaluation of outcomes for continuous quality improvement [52].

A clinical protocol is a written framework for the expected management path and outcome for a patient undergoing a particular procedure. Clinical protocols and care pathways are being widely implemented in the National Health Service (NHS), and although concerns were initially expressed regarding the lack of evidence for their efficacy [53,54], recent work has helped to address this issue. It would appear that both are capable of improving quality of care and patient satisfaction [55]. The aim of a clinical protocol is to improve the quality of care, and ensure that treatment is based on the latest evidence and research. They should complement rather than abolish intuitive thought based on clinical expertise. Education and training strategies are essential to support understanding, ownership and acceptance [56].

Decision analysis is the application of structured, quantitative methods to analyse decisions under conditions of uncertainty [57]. They can be shown graphically as decision trees and help to structure problems and highlight areas for further research. Decision analysis works on the principle that the degree of uncertainty decreases when the medical literature includes directly relevant and valid evidence [58].

## **Materials and methods**

#### *Protocol development*

On 15 June 2004, the IARC issued a press release classifying formaldehyde as carcinogenic to human beings [51]. This information was circulated to all consultants in paediatric dentistry and resulted in the withdrawal of Buckley's formocresol and all para-formaldehyde-containing devitalising pastes from the majority of teaching hospitals. In the Department of Child Dental Health, Newcastle Dental Hospital, Newcastle upon Tyne, UK, a specialist group of

**Table 1.** Comparison of alternatives to formocresol for pulp therapy: (MTA) mineral trioxide aggregate; (IPT) indirect pulp therapy; and (BMP) bone morphogenic protein.

Material	Clinical success (example cited)	Human clinical studies?	Tested against formocresol?	Operator ease of use	Patient acceptability	Cost of technique	Effect upon pulp cell
Glutaraldehyde	82% over 25 months Fuks <i>et al.</i> [73]	Yes	Yes	Good	Good	Low	Devitalisation
Electrosurgery	99.4% over 70 months Mack and Dean [74]	No	No	Poor	Poor	Medium	Devitalisation
Ferric sulphate	92% over 4 years Ibrecevic [60]	Yes	Yes	Good	Good	Low	Preservation
Calcium hydroxide	77.1% over 22.5 months Waterhouse [50]	Yes	Yes	Good	Good	Low	Preservation
MTA	100% over one year (grey) 84.2% over one year (white) Agamy <i>et al.</i> [75]	Yes	No	Fair	Good	High	Preservation
Lasers	100% over 90 days Elliot <i>et al.</i> [76]	Yes	Yes	Poor	Poor	High	Preservation
IPT	95% over 2–72 weeks Al Zayer <i>et al.</i> [77]	Yes	Yes	Good	Good	Low	Remineralisation
BMP	No studies	No	No	Unknown	Unknown	Unknown	Remineralisation
Collagen	No studies	No	No	Unknown	Unknown	Unknown	Remineralisation
Pulpectomy	91% over 36 months Casas and Kenny [61]	Yes	Yes	Poor	Poor	Low	Extirpation
Ledermix	79% over 42 month Hansen <i>et al.</i> [78]	Yes	No	Good	Good	Low	Preservation

paediatric dentists, comprising consultants, specialist registrars, university academics and a staff grade, was formed in order to establish a consensus decision on the management of extensively carious primary molar teeth.

A traditional narrative literature review was completed (Part I of this publication) and primary research papers for each of the possible alternatives to formocresol were identified. Where possible, randomised control trials were chosen to evaluate clinical and radiographic success for each medicament [59–65]. Histological animal studies were identified to enable comparison between the cytological and toxicological effects of different medicaments and techniques [66,67]. Each clinician in the specialist group was asked to critically appraise their allocated papers and to present their findings at a ‘brainstorming’ session.

Following appraisal of the selected publications, the group discussed the ideal properties of a pulp therapy agent and tabulated the key findings of the review (Table 1). It was felt that, in light of the recent IARC findings, it was necessary to implement the chosen alternatives as soon as possible, whilst also considering techniques which may be possible in the future.

For inclusion in the protocol, it was necessary for a technique or medicament to have a sufficient evidence base, ideally human trials, for clinical efficacy and to be economical in order to justify its routine use within an NHS teaching hospital. There should also be little immediate financial outlay or training implications to allow rapid introduction of the protocol.

On this basis, ferric sulphate (Astringent, Ultradent Products Inc., South Jordan, UT, USA) was chosen for use in the vital primary molar pulpotomy. Although concerns were expressed that this agent may mask underlying pulp pathosis, it was felt that it was clinically successful, operator- and patient-friendly, and a financially viable medicament. Mineral trioxide aggregate (MTA; Pro Root, Dentsply, Tulsa Dental, Weybridge, UK) will also be an option for staff-performed pulpotomies and perhaps introduced into the undergraduate arena in the future.

A working draft of the protocol was produced and circulated to enter into the ‘iterative’ process of review. The draft protocol consisted of a flow chart to assist clinicians in their treatment planning, combined with a key points document to offer further information, and to standardise data for future research

and audit. Each draft version was then circulated for comment a further three times. This resulted in the working protocol (Fig. 1). To facilitate future audit of the protocol, every time pulp therapy is performed within the Department, a stamp will be used to record standardised information in the patient's notes; for example, the time taken to achieve haemostasis and the number of applications of ferric sulphate required. The information will also be recorded in a 'pulp therapy book'.

#### *Implementation of the protocol*

Undergraduate dental students were informed of changes in protocol via information uploaded within the University Virtual Learning Environment. In addition, a lecture was given to all third-year students prior to their initial clinical sessions within paediatric dentistry, and an existing seminar was revised to include an update on pulp therapy in the primary dentition. The same information was supplied to all teachers of paediatric dentistry within the school and in outreach clinics. It is expected that further modifications to the teaching programme will be made as pulp therapy techniques are developed and audited.

The working protocol and key points document were circulated to all staff working within the department. Discussion of these documents was incorporated into the junior staff induction programme. Nursing staff were also informed of the new techniques and proposed local protocols via the senior nurse. Areas for future staff training were identified at the team meeting, and hands-on training for specialist staff has been arranged for the near future.

#### **Discussion**

Following the recent IARC press release [51], the use of formocresol in paediatric dentistry is no longer recommended, and clinicians must adopt alternative evidence-based procedures. The authors acknowledge that the evidence for some of the alternatives to formocresol is weak. However, the IARC statement demands a change to current practice and an urgent review of the alternatives in order to develop an interim protocol. It is hoped that this protocol will add to the debate and enable the collection of standardised data which will, in turn, lead to a more evidence-based guideline in the future.

The importance of careful patient and tooth selection when considering provision of a pulp therapy cannot

be overemphasised. In order for vital pulp therapy to be successful, the patient must be sufficiently compliant to allow adequate moisture control, ideally with rubber dam placement, and the tooth must be radiographically free of pathology, and restorable with a bonded restoration or preformed metal crown in order to provide an effective seal.

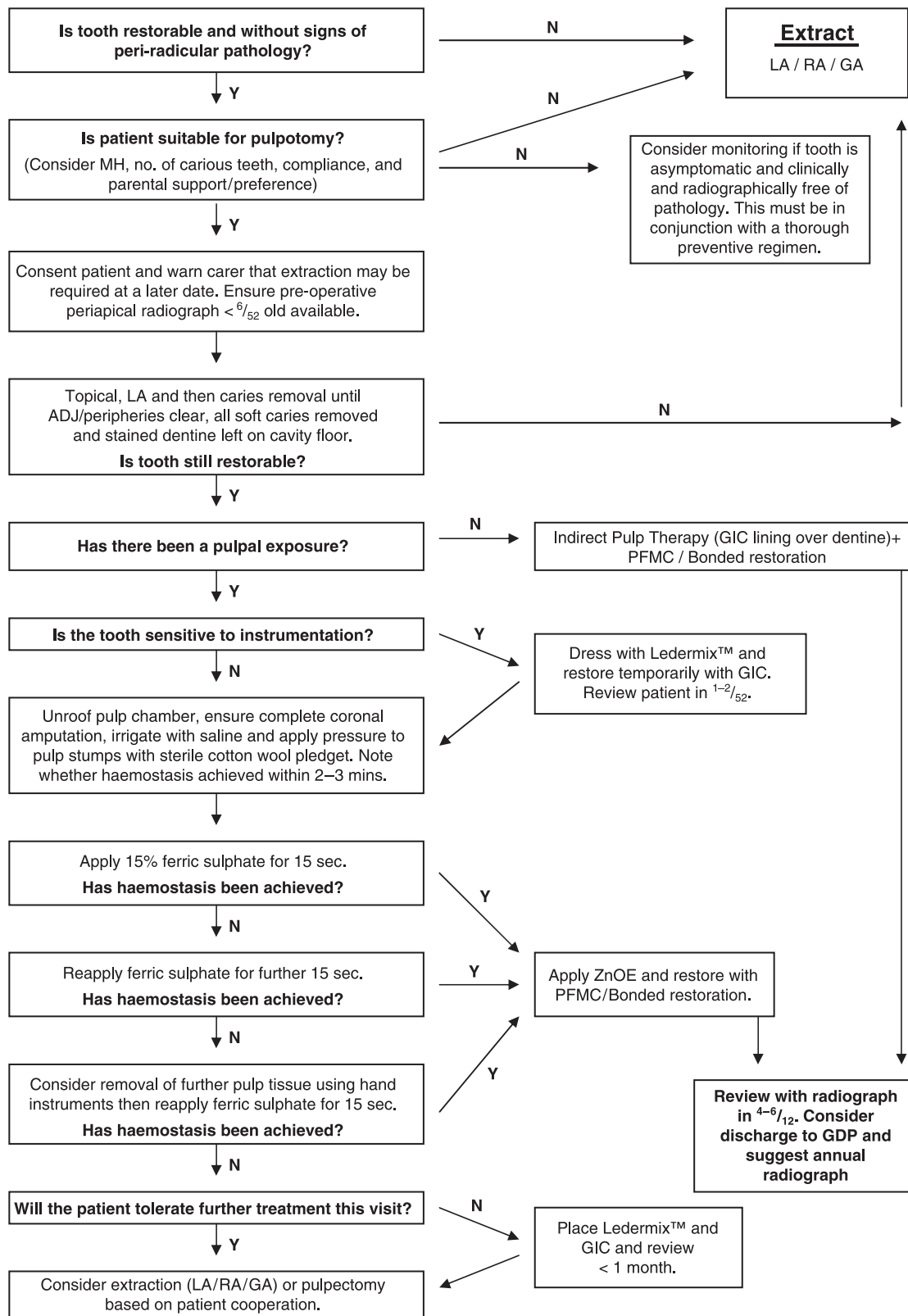
Despite careful initial assessment, diagnosis of pulpal status may be difficult. For example, once an irreversibly inflamed coronal pulp has been amputated, the health of the radicular pulp is assessed on an empirical basis, i.e. how readily the pulp stump bleeds. As yet, we have no scientific clinical method of determining pulpal status prior to treatment, although there has been some work to investigate correlations between the presence of certain inflammatory mediators and clinical outcome [68,69].

Presently, in Newcastle, the treatment of choice for nonvital primary molars is extraction since there is little evidence of an alternative medicament which is as effective as formocresol and which exhibits minimal technique sensitivity. Pulpectomy remains an option for the future, but staff training will be required before the technique can be introduced in the clinical setting and taught at undergraduate level. The management of the partially vital primary molar merits further research and discussion since the evidence is scant for the use of Ledermix™ (Blackwell Supplies Ltd, Gillingham, UK) in such teeth.

In order to justify its use within an NHS teaching hospital, a medicament must be effective from both a clinical and an economical perspective. Mineral trioxide aggregate has been previously excluded in some centres on the basis of its expense, but research would suggest that MTA does have a role to play in the treatment of carefully selected primary molar vital pulpotomies and that its cost is comparable to that of ferric sulphate.

Ferric sulphate appears to be as effective in vital pulpotomies as formocresol, and there is no evidence to date to suggest any adverse effects of this medicament. As such, within the protocol, it was chosen as the treatment of choice for vital pulpotomies. Further research and audit is required to build on the existing evidence base for ferric sulphate, in particular the authors would welcome more long-term randomised clinical trials.

It has been suggested that the careful monitoring of primary teeth with extensive caries is a reasonable treatment option when combined with a thorough preventive regimen [70,71]. The authors suggest that



**Fig. 1.** Primary molar protocol: (MH) medical history; (LA) local anaesthesia; (RA) relative analgesia; (GA) general anaesthesia; (ADJ) amelodentinal junction; (GIC) glass ionomer cement; (ZnOE) zinc oxide eugenol cement; (PFMC) preformed metal crown; and (GDP) general dental practitioner.

monitoring may be appropriate, but only for patients who are unable to accept operative treatment, and where the tooth is asymptomatic, and clinically and radiographically free of pathology. It is advisable that this decision is made with the consent of a fully informed parent because of the potential risk of damage to the permanent successor. Monitoring is not an option for patients to whom infection poses a significant risk; for example, those with leukaemia or congenital heart defects.

### *Radiographic review*

Regular radiographic monitoring of treated teeth is advocated to assist in the assessment of primary molar and permanent successor teeth. A radiograph taken after treatment would enable detection of recurrent caries, a failing coronal restoration, peri-apical or furcal radiolucencies, internal or external root resorption, failure of eruption of the permanent successor tooth along its expected path, and pathosis, with or without concomitant clinical symptoms which may damage or deflect the permanent tooth germ [50].

Although the literature relating to the frequency of radiographing pulpotomised teeth is scant, the Faculty of General Dental Practitioners [72] clearly outlines selection criteria for radiographic screening according to caries risk status. These guidelines suggest that bitewing radiographs should be taken on a 6-monthly basis for children identified as high caries risk and on an annual basis for those classified as moderate risk. The authors would suggest that a

vertical bitewing radiograph could be taken as part of this radiographic review because this would enable a review after pulp therapy without an increase in radiation dose.

### **Conclusion**

Following a review of the current literature, a working clinical protocol for pulp therapy techniques in the extensively carious primary molar has been developed. This protocol has been implemented at the undergraduate and postgraduate levels, and has helped to identify areas where further staff training is required. It is expected that the clinical protocol will evolve as further evidence comes to light.

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#### **What this paper adds**

- This paper highlights the stages in the development of a local clinical protocol.
- The protocol consisted of a flow chart to assist clinicians in their treatment planning combined with a key points document to offer further information and to standardise data for future research and audit.

#### **Why this paper is important for paediatric dentists**

- Prior to the use of any clinical intervention the evidence base behind it requires consideration.
- In order to justify its use within any clinical setting (be it primary dental care or an NHS teaching hospital) a medicament or technique must be effective from a clinical and economical perspective.
- Ferric sulphate was chosen within our protocol as the treatment of choice for vital pulpotomies as it appears to be as effective as formocresol in vital pulpotomies to date and there is no evidence to suggest any adverse effects from this medicament.

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