

# Clearance of a topically applied fluorescein gel from periodontal pockets

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Oosterwaal PJM, Mikx FHM and Renggli HH: Clearance of a topically applied fluorescein gel from periodontal pockets. *J Clin Periodontol* 1990; 17: 613-615.

**Abstract.** The clearance of a fluorescein gel applied with an irrigation technique in periodontal pockets was studied. In order to evaluate the time a drug remains in a periodontal pocket, the alteration in concentration of this drug in a given time period was investigated. After application of the gel in 4 pockets of 10 patients, samples were taken from 1 of the 4 pockets at 5, 10, 20 and 40 min. The results show that in the 1st phase, directly after application, most of the gel disappeared from the pocket, while in the 2nd phase, the fluorescein gel is washed out with a calculated 50% reduction time of 12.5 min. The rapid clearance of the gel observed after irrigation might provide a partial explanation of the minor effect of pocket irrigation on the subgingival microflora.

Key words: clearance; fluorescein cellulose gel; periodontal pocket.

Accepted for publication 12 September 1989

In the treatment of periodontitis, antibiotics and disinfectants are used to suppress subgingival bacteria. Apart from systemic administration of antibiotics, antimicrobial drugs may be delivered directly into the periodontal pocket thereby providing the possibility of using drugs unsuitable for systemic use (Addy 1988). Moreover, by local application, drugs may be applied at higher and bactericidal concentrations. Methods have been developed to carry agents directly to the periodontal pocket. Used delivery methods are irrigation of the pocket by a fluid or gel containing antimicrobials, or slow release devices such as fibres and acrylic strips impregnated with antimicrobials and placed in the pocket for a period of time (for review, see Dubrez (1989)).

Irrigation with stannous fluoride or chlorhexidine without preceding debridement has only a limited and transient effect on spirochetes and motile rods (Mazza et al. 1981, Haskel et al. 1986, Lander et al. 1986, Wennström et al. 1987). After scaling and rootplaning, irrigation with chlorhexidine does not augment the effect of mechanical debridement on microscopical and clinical parameters (Khoo & Newman 1983, Braatz et al. 1985, Mac Alpine et al. 1985, Wennström et al. 1987). The effect of an antimicrobial drug depends on its concentration and contact time. Recently, minimal bactericidal concen-

trations at short contact times of antimicrobials used in periodontal therapy were determined (Caufield et al. 1987, Oosterwaal et al. 1989). The length of time a drug applied by irrigation will remain in a periodontal pocket appears to be unknown. The fluid flow found in such pockets (Waerhaug 1952; Valazza et al. 1972; Cimasoni 1983; Villela et al. 1987) could possibly reduce the concentration of a topically applied drug substantially.

In the present study, the clearance of a sodium fluorescein cellulose gel applied in human periodontal pockets was investigated.

## Material and Methods

10 subjects, 1 male and 9 female, mean age 38 years, with advanced periodontal destruction, consented to participate in this study. They were selected on the basis of the presence of at least 4 interdental periodontal pockets of 5-9 mm involving single root teeth. In the experimental design, the criteria of a randomised double-blind, controlled clinical trial were followed in order to exclude disturbing factors as much as possible (Pocock 1983). In each pocket, a fluorescein gel pH 7.8 containing 1% w/v sodium fluorescein, 0.8% w/v sodium chloride and 0.5% w/v hydroxypropylmethylcellulose 4000 cP in H<sub>2</sub>O, was placed in the pockets, buccal to the

contact points. The applications were performed by one operator using a syringe with a blunted needle with diameter of 0.65 mm placed near the bottom of the pocket until the fluorescein gel became visible at the entrance of the pocket. Subsequently, absorbent paper points (nr. 50 Kerr, Basel, CH) were carefully placed at the bottom of the pockets and sequentially removed from 1 of the 4 selected pockets at 5, 10, 20 and 40 min after application of the sodium fluorescein gel. Thus, in every patient each pocket was sampled only once. In order to investigate the spreading of the gel in the pocket, sampling was performed not only at the buccal side, where the gel was applied, but also at the lingual side of the contact point where no gel was applied.

After drying of the paperpoints at 37°C for 1 h, the points were cut to 4 mm lengths and placed into vials containing 1 ml 0.2 M phosphate buffer pH 7.2. The fluorescence of these vials measured on a scale from 0-1000 was determined by another operator using a fluorimeter (LS-5 Perkin-Elmer, Beaconsfield, UK) at an excitation of 480 nm and an emission of 510 nm. The concentration of the fluorescein gel in the periodontal pockets was estimated by the use of a calibration curve. The calibration curve was made by using paperpoints soaked in a series of fluorescein gel solution in phosphate buffer

Table 1. Fluorescence (scale 0–1000) of paperpoints samples taken buccal and lingual of the contact point at different time intervals after application of a 1% sodium fluorescein gel at the buccal side of interdental pockets of 5–9 mm

Patient	Buccal samples				Lingual samples			
	(min)				(min)			
	5	10	20	40	5	10	20	40
A	1000* (7)**	218 (7)	216 (7)	78 (7)	1000* (7)	156 (5)	945 (6)	59 (7)
B	32 (7)	265 (9)	27 (7)	6 (7)	13 (5)	417 (7)	20 (7)	6 (7)
C	638 (8)	1000* (8)	1000* (9)	120 (7)	46 (5)	1000* (7)	1000* (7)	176 (5)
D	880 (7)	189 (7)	36 (7)	25 (8)	10 (7)	425 (8)	60 (7)	171 (6)
E	1000* (7)	1000* (8)	80 (7)	275 (7)	888 (7)	1000* (9)	367 (5)	315 (7)
F	1000* (5)	59 (6)	1000* (5)	744 (6)	1000* (6)	626 (5)	1 (5)	2 (5)
G	279 (8)	99 (7)	1000* (7)	10 (8)	122 (5)	286 (6)	622 (6)	57 (7)
H	143 (7)	313 (7)	296 (8)	21 (8)	106 (6)	862 (7)	358 (6)	17 (7)
I	131 (8)	470 (8)	71 (6)	204 (7)	1000* (7)	82 (7)	260 (5)	1 (5)
J	1000* (7)	596 (7)	106 (7)	38 (7)	1000* (7)	1000* (6)	312 (7)	112 (6)
Median	759	289	161	58	505	526	335	58
Range	1000* – 32	1000* – 59	1000* – 27	744 – 6	1000* – 10	1000* – 82	1000* – 1	315 – 1

\* Exceeding the scale of measurement. \*\* ( ) mm probing depth.

in a concentration range of 300 to 0.3 nmol ml<sup>-1</sup>. The fluorescence of these paperpoints was determined as described above.

## Results

The fluorescence (scale 0–1000) of the paper point samples taken buccal and lingual of the contact point at different time intervals after application of the sodium fluorescein gel is presented in Table 1. The samples with a fluorescence exceeding the scale of measurement were given a value of 1000.

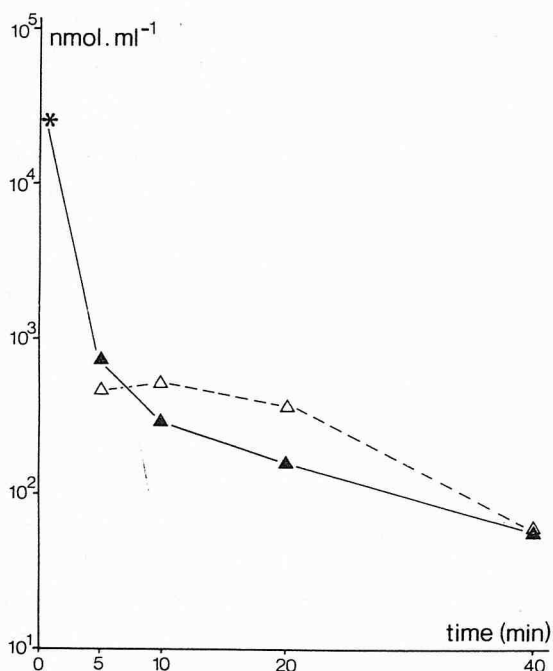


Fig. 1. Median concentrations of sodium fluorescein in pockets 5, 10, 20 and 40 min after application. Fluorescein gel was applied at the buccal side of the interdental pockets, while measurements were performed at both the buccal and lingual sides.

\*Concentration in the gel. ▲ Buccal side. △ Lingual side.

The fluorescence values showed a large variation. Fluorescence values exceeding the scale of measurements were found in 4 of the 10 pockets sampled at 5 min, in 2 of the 10 pockets sampled at 10 min and in 3 of the 10 pockets sampled at 20 min. High and low values were observed in different pockets of the same patient (F, G) at different time intervals. There was no indication of a correlation between pocket probing depth and the amount of fluorescence.

The median fluorescence values were calculated due to the large variation. At the buccal sides, the median fluorescence was 759, 5 min after application, 289, 10 min after application, 161, 20 min after application and 58, 40 min after application. At the lingual sides, the median fluorescence was 105, 5 min after application, 526, 10 min after application, 335, 20 min after application and 58, 40 min after application.

The median fluorescence values of each time interval were used for calculation of the median concentration of sodium fluorescein in the paperpoints samples by the use of a calibration curve as described in *Material and Methods*. Fig. 1 shows the decrease of the concentration of fluorescein gel from the pockets. The concentration indicated at time zero represents the concentration in the applied fluorescein gel. The figure shows that within the first 5 min. most of the gel disappeared from the pocket, while in a later phase, the fluorescein gel is washed out with a calculated 50% reduction time of 12.5 min.

The gel applied buccal of the contact point was also observed at the lingual sides of the interdental pocket. The median concentrations at the lingual side

corresponded to those found at the buccal side and decreased at a similar rate.

## Discussion

Fluorescein gel applied in human periodontal pockets was chosen as a model to estimate the clearance of a gel applied by irrigation. The lower the clearance, the longer the time a drug remains in the pocket. The clearance depends upon the physical and chemical properties of the drug and upon the mechanical behavior of the periodontal pocket. Gel applied buccal to the contact point diffuses to the lingual side where it is gradually released. High concentrations of fluorescein gel were still present in 3 pockets, 20 min after application and in 2 pockets, 10 min after application and in 4 pockets 5 min after application. This suggests that not all investigated pockets reacted in the same way. However, in most sites, the concentration of the gel in the pockets decreased with increasing time interval.

For the interpretation of the data, median values were chosen to reduce the wide individual variations. The median values of the concentration of the sodium fluorescein gel decreased markedly in the first few minutes. This decrease is probably due to the elastic behaviour of the soft tissues of the pocket, to bleeding after application and also as a result of spreading of the gel to the lingual side. About 10 min after application, a steady decrease of the median concentration of the applied fluorescein gel was observed. This decrease is linear on a logarithmic scale and enabled estimation of the 50% washing out time

(12.5 min) of the fluorescein gel. It is likely that in this phase, the gel disappears by the fluid flow through the pocket together with a gradual release from the adherent surfaces. This phenomenon of washing out could be the explanation for the limited effect of local irrigation on subgingival microorganisms.

Apart from the contact time, the bactericidal effect of a drug depends on its concentration. However, the concentration of established antimicrobials used for irrigation of periodontal pockets is mostly too low to be bactericidal (Caufield et al. 1987; Oosterwaal et al. 1989).

The results of the present study indicate that after irrigation, the bulk of a drug applied in the form of fluorescein gel disappears from most of the pockets within a few min, while in a later phase, the applied gel is gradually washed out. The observed rapid clearance of this gel after local application might at least partly be the reason for the limited effect of pocket irrigation on the subgingival microflora.

#### Acknowledgement

The authors wish to express their appreciation to Gordon Wolffe for correcting the English and syntax and to Els Smit for typing this manuscript.

#### Zusammenfassung

*Die Clearance eines lokal eingebrachten Fluoresceingels aus parodontalen Taschen.*

Die Clearance eines mit einer Taschenspülung eingebrachten Fluoresceingels wurde studiert. Um die Zeit, die ein Medikament in einer parodontalen Tasche verbleibt zu messen, wurde die Veränderung der Konzentration dieses Medikamentes während einer vorgegebenen Zeitperiode untersucht. Nach der Applikation des Gels in 4 Taschen bei 10 Patienten wurden nach 5, 10, 20 und 40 Minuten von 1 der 4 Taschen Proben entnommen. Die Ergebnisse zeigen, daß in der ersten Phase, direkt nach der Applikation, der größte Teil der Geles aus der Tasche verschwand, während in der zweiten Phase das Gel mit einer berechneten Halbwertszeit von 12.5 Minuten ausgewaschen wurde. Die schnelle Clearance des Geles nach der Spülung könn-

te teilweise den geringen Effekt einer Taschenspülung auf die subgingivale Mikroflora erklären.

#### Résumé

*Clearance à partir des poches parodontales d'un gel à la fluorescéine appliqué localement*  
Cette étude concerne la clearance d'un gel à la fluorescéine appliqué dans les poches parodontales par irrigation. Pour évaluer combien de temps un médicament subsiste dans une poche parodontale, nous avons étudié les changements de concentration de ce médicament au cours d'une période d'une longueur donnée. Après application du gel dans 4 poches chez 10 patients, des prélèvements ont été faits à 5, 10, 20 et 40 min. Les résultats montrent que, dans la 1<sup>ère</sup> phase, juste après l'application, la plus grande partie du gel disparaît de la poche, tandis que, dans la 2<sup>ème</sup> phase, le gel à la fluorescéine disparaît par dilution, à une vitesse correspondant à 50% de réduction pour 12.5 min. La rapidité de la clearance observée pour le gel après irrigation peut donner une explication partielle des effets mineurs de l'irrigation des poches sur la flore microbienne sous-gingivale.

#### References

- Addy, M. Rational for chemotherapy in the treatment of periodontal disease (1988). *Periodontology Today*. International Congress Zürich, pp. 281–289. Basel: S. Karger.
- Braatz, L., Garrett, S., Claffey, N. & Egelberg, J. (1985) Antimicrobial irrigation of deep pockets to supplement non surgical periodontal therapy. II Daily irrigation. *Journal of Clinical Periodontology* **12**, 630–638.
- Caufield, P. W., Allen, D. N. & Childers, N. K. (1987) In vitro susceptibilities of suspected periodontopathic anaerobes as determined by membrane transfer assay. *Antimicrobials and Agents Chemotherapy* **12**, 1989–1993.
- Cimasoni, G. (1983) *Crevicular fluid updated*. Monographs in oral science, vol. 12, ed. Meyers, H. M., Basel: S. Karger.
- Dubreux, B. (1989) Médicaments dans la poche parodontale. Une revue de la littérature. *Revue Mensuelle Suisse Odonto-Stomatologique* **99**, 149–161.
- Haskel, E., Esquenasi, J. & Yussim, L. (1986) Effects of subgingival chlorhexidine irrigation in chronic moderate periodontitis. *Journal of Periodontology* **57**, 305–310.
- Khoo, J. G. L. & Newman, H. N. (1983) Subgingival plaque control by a simplified oral hygiene regime plus local chlorhexidine or metronidazole. *Journal of Periodontal Research* **18**, 607–619.
- Lander, P. E., Newcomb, G. M., Seymour, G. J. & Powell, R. N. (1984) The antimicrobial and clinical effects of a single subgingival irrigation of chlorhexidine in advanced periodontal lesions. *Journal of Clinical Periodontology* **13**, 74–80.
- MacAlpine, R., Magnusson, I., Kiger, R., Crigger, M., Garrett, S. & Egelberg, J. (1985) Antimicrobial irrigation of deep pockets to supplement oral hygiene instruction and root debridement. *Journal of Clinical Periodontology* **12**, 568–577.
- Mazza, J. E., Newman, M. G. & Sims, T. N. (1981) Clinical and antimicrobial effect of stannous fluoride on periodontitis. *Journal of Clinical Periodontology* **8**, 203–212.
- Oosterwaal, P. J. M., Mikx, F. H. M., Van den Brink, M. E. & Renggli, H. H. (1989) Bactericidal concentrations of chlorhexidine-digluconate, amine fluoride gel and stannous fluoride gel for subgingival bacteria tested in serum at short contact times. *Journal of Periodontal Research* **24**, 155–160.
- Pocock, S. J. (1983) *Clinical trials* New York: Wiley, J. & Son.
- Valazza, A., Matter, J., Ogilvie, A. & Cimasoni, G. (1972) Fluide gingivale, inflammation gingivale, profondeur des poches et perte osseuse. *Revue Mensuelle Suisse Odonto-Stomatologie* **82**, 824–832.
- Villela, B., Cogen, R. B., Bartolucci, A. A. & Birkedal-Hansen, H. (1987) Crevicular fluid collagenase activity in healthy, gingivitis, chronic adult periodontitis and localized periodontitis patients. *Journal of Periodontal Research* **22**, 209–211.
- Waerhaug, J. (1952) The gingival pocket. Anatomy, pathology, deepening and elimination. *Odontologisk Tidskrift* **60**, suppl. 1, 1–186.
- Wennström, J. L., Dahlén, G., Gröndahl, K. & Heijl, L. (1987) Periodic subgingival antimicrobial irrigation of periodontal pockets II. Microbiological and radiographical observations. *Journal of Clinical Periodontology* **14**, 573–580.

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