

logic analyses were made 8 to 14 hours following the last rinse.⁶ The metabolic activities of the organisms within the dental plaque, measured by the enzymatic breakdown of fermentable sugars, were also demonstrated to be effectively inhibited in a group of subjects who had used a 0.1 per cent hexetidine rinse 10 to 14 hours before being tested.⁴ Similarly, another investigator reported significant reductions in mouth odor and oral flora when determinations were made 8 to 10 hours following a rinse with this antiseptic preparation.⁷

Human and animal toxicity studies have shown hexetidine to be safe when administered for extended periods of time.^{6, 8}

In a study of 297 patients, in which fourteen dentists participated, Kimmelman⁹ reported the hexetidine oral antiseptic to be a major aid in reducing the inflammatory symptoms of bleeding, redness, and pain. In this study home therapy consisted of a twice-daily rinse; at the dental chair, hexetidine 0.1 per cent solution was administered by swab or syringe spray. It was also used as an irrigating solution accompanying scaling procedures, as a pre- and post-operative rinse for extractions and minor oral surgery, and for acute and chronic gingival lesions. Lisanti⁶ reported considerably less bleeding following periodontal instrumentation and better healing when hexetidine antiseptic was used as a twice-daily home rinse in a controlled series of periodontal patients. The previously cited study utilized the half-mouth technique, and the results of rinsing with the hexetidine solution could be favorably compared to those obtained with a placebo rinse.

CLINICAL PROCEDURE

The present study extended over a period of more than 15 months and included 220 patients, all of whom required surgical treatment for their periodontal conditions. The most frequently performed surgical procedures were gingivectomies. A few mucogingival flap operations, osteoplasties, and vestibular resections were also included. The surgical procedures utilized were those described by Sorrin.¹⁰

At random, 108 patients were selected to use the hexetidine solution as an oral rinse, $\frac{1}{2}$ ounce (one measuring tablespoonful) retained in the mouth for $\frac{1}{2}$ minute twice daily (morning and evening). The same solution was also sprayed with the dental unit spray apparatus over the site of operation upon completion of the surgical procedure and prior to the application of the zinc oxide-eugenol periodontal pack.

As a control, 112 patients used a normal saline solution in the same manner. In this group, the hexetidine solution was not sprayed on the operative site prior to the application of the periodontal pack.

In half of the patients of each group the periodontal packs were removed at the end of 7 days. Many of these patients, however, required placement of a second pack in order to avoid discomfort. The remaining patients in each group retained their periodontal packs for 8, 9, 10, 12, and 14 days, respectively.

Kodachrome photographs were taken of random representatives of each group. All subjects were checked for (1) clinical appearance of healing, (2) odor, and (3) patient's subjective response.

BACTERIOLOGIC PROCEDURE

A bacteriologic survey was made of the microorganism resident under the periodontal pack in six of the control or saline-rinse patients and in nine of the active or hexetidine group of patients. The swab technique was used, and the cultures obtained were inoculated on blood agar plates, MacConkey plates, in thioglycolate broth, and on mitis salivarius plates. When necessary, other differential media were used for bacteriologic isolation and identification.

CLINICAL RESULTS

The use of the 0.1 per cent hexetidine antiseptic oral rinse as directed accelerated healing so that a 1 week postoperative result frequently appeared clinically comparable to the 2 week postoperative result obtained in patients of the control or saline-rinse group. In many of these patients the tissues appeared to be fully healed at the end of 1 week, although 1 week was frequently inadequate to provide a degree of healing sufficient to permit the patient to be comfortable without the protection of a periodontal pack. For the average patient, a period of 10 days to 2 weeks was found to be the desirable time for pack retention. However, this time varied with (1) the nature and extent of the surgical procedure, (2) the inherent "healing potential" of the patient, (3) the oral microbial flora, (4) the operative technique employed, and (5) the oral hygiene practices of the patient.

A definite correlation was found between odor and extent of healing. With some experience one could predict that, in the hexetidine group, when marked odor and inadequate healing were observed, the hexetidine solution had not been used as directed; the patient had either rinsed only once daily or used an insufficient quantity of solution for each rinse.

The amount of hexetidine solution which remained in each patient's test sample bottle at the time of pack removal was found to be a fair measure of (1) the intensity of odor and (2) the "rawness" of the operative site.

The marked redness and the granular appearance of the tissues in the postoperative saline-rinse group is apparent when compared with the hexetidine group. This is illustrated graphically in Figs. 1 and 2, which present visual evidence comparing the saline-rinse group with the hexetidine group under similar circumstances of surgical procedure, surgical technique, and postoperative treatment.

The saline rinse was found to be capable of achieving beneficial results if repeated very frequently (on an hourly basis) throughout the day. However, this was not a practical procedure for most patients. Furthermore, frequent saline rinses increased the risk of dislodgment or premature accidental removal of the periodontal pack.

Fig. 1.—Photographs on left show results with Hexetidine rinse; those on right show results with saline rinse.

A, Seven days after operation.	B, Seven days after operation.
C, Seven days after operation.	D, Fourteen days after operation.
E, Seven days after operation.	F, Seven days after operation.
G, Nine days after operation.	H, Eight days after operation.



Fig. 1.—(For legend, see opposite page.)

TABLE I

PATIENT NO.	POSTOPERATIVE INTERVAL (DAYS)	GROUP	QUANTITATIVE TOTAL BACTERIAL ESTIMATION*	ORGANISMS ISOLATED†	DIRECT SMEAR, GRAM STAIN
1	14	Control	4+	<i>Streptococcus viridans</i> † Nonhemolytic streptococcus <i>Neisseria catarrhalis</i>	Fusiform bacilli, a few Spirilleae, gram-positive and gram-negative cocci
2	14	Control	4+	<i>Streptococcus viridans</i> † Nonhemolytic streptococcus Diphtheroids	Fusiform bacilli, lactobacilli, gram-positive cocci
3	14	Control	4+	<i>Streptococcus viridans</i> † <i>Pseudomonas aeruginosa</i> † Nonhemolytic streptococcus	Fusiform bacilli, gram-positive cocci, gram-negative bacilli
4	14	Control	3+	<i>Streptococcus viridans</i> <i>Staphylococcus albus</i> Nonhemolytic streptococcus <i>Hemophilus influenzae</i>	Fusiform bacilli, gram-positive cocci
5	11	Control	3+	<i>Staphylococcus aureus</i> † <i>Streptococcus viridans</i> Nonhemolytic streptococcus	Fusiform bacilli, few gram-positive cocci
6	14	Control	3+	<i>Enterococcus</i> † Few <i>Candida</i> species	Rare gram-positive cocci
7	14	Sterisol	3+	<i>Bacterium paracoli</i> † Nonhemolytic streptococcus <i>Streptococcus viridans</i>	Lactobacilli, fusiform bacilli, gram-negative bacilli, gram-positive cocci
8	14	Sterisol	3+	Nonhemolytic streptococcus† <i>Staphylococcus albus</i> <i>Streptococcus viridans</i>	Scanty number of bacteria seen, few fusiform bacilli, few gram-positive cocci
9	7	Sterisol	4+	<i>Streptococcus viridans</i> † Nonhemolytic streptococcus <i>Bacterium paracoli</i> <i>Staphylococcus albus</i>	Few gram-negative bacilli, few gram-positive cocci in pairs
10	14	Sterisol	4+	Cultures overgrown by <i>Proteus</i> sp.; few enterococci	Rare gram-negative bacilli
11	12	Sterisol	3+	<i>Aerobacter</i> species,† enterococcus, few nonhemolytic streptococcus	Rare gram-negative bacilli
12	14	Sterisol	3+	<i>Neisseria catarrhalis</i> ,† aerobacter species,† few <i>Staphylococcus albus</i> , diphtheroids	Gram-negative cocci; gram-positive cocci; gram-negative bacilli
13	14	Sterisol	3+	<i>Escherichia coli</i> ,† few enterococcus, few <i>Staphylococcus albus</i>	Rare gram-negative bacilli
14	14	Sterisol	4+	<i>Aerobacter</i> species,† enterococcus	Gram-positive cocci in chains; few gram-negative bacilli, lactobacilli
15	14	Sterisol	4+	<i>Aerobacter</i> species,† enterococcus, few <i>Streptococcus viridans</i>	Rare gram-negative bacilli

*Quantitative estimation, with 4+ as the highest evaluation, based on the confluency of total growth in all sectors of an eight-part plate.

†Predominating organism. The bacteria are listed in order, with the most prevalent organism in first place.

Six of the patients in the active medication group reported a mild burning sensation while the hexetidine solution was retained in the mouth. Two patients indicated that the hexetidine solution was "too strong" and did not continue its use. However, in no patients in the hexetidine group were objective adverse effects observed. Acceptance by patients was excellent, and most patients expressed a desire to continue the use of the antiseptic oral rinse after completion of their treatments.

BACTERIOLOGIC RESULTS

The results of the bacteriologic survey (Table I) indicated a predominance of gram-positive organisms, particularly *Streptococcus viridans*, in the control or saline-rinse group, whereas in the active or hexetidine solution group only one patient evidenced a predominance of *Streptococcus viridans*. In the control group five of the six subjects surveyed yielded the gram-negative fusiform bacillus. In the active medication group only two of the nine patients surveyed yielded fusiform bacillus in their culture samples.

All of the subjects in whose culture samples fusiform bacillus was isolated presented the typical fetid odor commonly associated with the periodontal pack. They also experienced relatively delayed healing. The fetid oral odor was present in the major portion of the control or saline-rinse group. The two subjects in the active or hexetidine group who evidenced fusiform bacillus also had the same associated fetid odor. In these two subjects inadequate or infrequent use of the hexetidine rinse may have been the cause of this finding. The fusiform bacillus is an odor-producing organism. In small numbers these bacilli are part of the "normal" oral microbial flora. The fusiform bacillus is one of the "Vincent's infection" organisms found in necrotizing ulcerative gingivitis and contributes to the unique fetid odor of that disease.

DISCUSSION

A 0.1 per cent hexetidine antiseptic solution, applied via the dental spray apparatus to the operative site prior to placement of the periodontal pack and used as a twice-daily home oral rinse, accelerated healing following periodontal surgical procedures when compared to a control or saline oral rinse. Used in this manner, hexetidine effectively controlled the fetid odor usually associated with periodontal packs; in many cases odor was completely absent. Although in a large number of cases the time required for retention of the periodontal pack appeared to be reduced, it is difficult to assess these results objectively, since surgical technique, extent of surgical procedure, and individual healing potential are variables that are difficult to relate. Subjectively, most patients

Fig. 2.—Photographs on left show results with Hexetidine rinse; those on right show results with saline rinse.

A, Seven days after operation.	B, Seven day after operation.
C, Fourteen days after operation.	D, Fourteen days after operation.
E, Seven days after operation.	F, Seven days after operation.
G, Eight days after operation.	H, Twelve days after operation.

A.



B.



C.



D.



E.



F.



G.



H.



Fig. 2.—(For legend, see opposite page.)

indicated increased comfort during the postoperative period and better tolerance for the periodontal pack.

A clinical correlation appeared to exist between the presence of fusiform bacilli, odor formation, and delayed postsurgical healing. This pathologic triumvirate appeared to be interrupted and reversed by the use of 0.1 per cent hexetidine rinse. This study therefore suggested further investigation into the relationship of bacteria, delayed healing, and postsurgical odor production under periodontal packs.

SUMMARY

A 0.1 per cent hexetidine antiseptic oral rinse was evaluated for its use as an immediate postoperative spray and as a twice-daily home rinse. Results with respect to healing, time needed for retention of the periodontal pack, and prevention of unpleasant odors associated with periodontal packs were evaluated and compared to a group of patients who underwent similar operative procedures and who used normal saline solution as an oral rinse. Kodachrome photographs provided visual evidence of the results obtained in both groups, and bacteriologic surveys in a limited number of subjects were also performed.

1. Healing of the periodontal tissues was accelerated in the 0.1 per cent hexetidine antiseptic oral rinse group when compared to the saline-rinse group.

2. The foul odor usually accompanying retention of the periodontal pack was effectively controlled. In the majority of cases the pack had *no* odor when removed.

3. Responses by patients indicated increased comfort and better tolerance for the periodontal pack.

4. A saline rinse was found to be capable of achieving beneficial results if repeated frequently, on an hourly basis, throughout the day. However, this increased the risk of periodontal pack dislodgment. Furthermore, most patients lacked the time needed for such frequent rinsing.

5. In each case in which the fusiform bacillus was isolated, the subject presented the typical fetid odor associated with the periodontal pack.

6. A clinical correlation appeared to exist between the presence of fusiform bacilli, odor formation, and delayed postsurgical healing. This pathologic triumvirate appeared to be interrupted and reversed by a 0.1 per cent hexetidine antiseptic oral rinse.

The bacteriologic portion of this study was performed by the staff of Fredrick B. Traub, M.D., Chief of Microbiology at the Jewish Hospital of Brooklyn.

REFERENCES

1. Read, R. R.: The Synthesis and Physical Chemical Properties of 1, 3 Disubstituted Hexahydropyrimidines, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
2. Church, B. D.: Inhibition of Metabolic Activities in Microorganisms by Hexetidine, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.

3. Lionetti, F. J.: The Metabolic Effects of Bis-1, 3 Beta Ethylhexyl, 5-Methyl 5-Amino hexahydropyrimidine on the Formed Elements of Human Blood, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
4. Fosdick, L. S.: Retention of Hexetidine on Dental Plaque and Oral Tissues, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
5. Dukes, C. D.: The In Vivo and In Vitro Antimicrobial Activity of Hexetidine and Homologues, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
6. Lisanti, V. F.: Effect of Continued Use of a Hexetidine Solution on the Bacterial Flora and Certain Enzyme Systems of Saliva, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
7. Lind, H. E.: Relationship of Bacterial Reductions to Mouth Odor After Oral Application of Hexetidine, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
8. Calandra, J. C.: The Acute and Chronic Toxicity of Hexetidine, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
9. Kimmelman, B. B.: The Effect of Hexetidine Preparations on Acute and Chronic Oral Diseases, Paper given at Hexahydropyrimidine Symposium, Northwestern University, October, 1958.
10. Sorrin, S.: The Practice of Periodontia, New York, 1960, McGraw-Hill Book Company, Inc.
11. Halvorson, H. O., and Gorman, J.: The Abnormal Pattern of Protein Synthesis in *Pseudomonas azotogensis* in the Presence of Hexetidine, *Exper. Cell Res.* 17: 522-524, 1959.
12. Fredell, W. G., White, R. C., and Sanders, R. G.: Topical Applications of a New Antibacterial Agent, *J. Am. Pharm. A.* 19: 428-431, 1958.
13. Quartero, Pietro: Clinical and Bacteriological Results on Parodontopathic Patients Treated With Hexetidine, *Stomatol. practica* 2: 11, 1960.
14. Esquivel, Eligio: The Use of a New Antiseptic, Hexetidine, in Otorhinolaryngology, *de Resumen Otolaryngol.* 2: 213-219, 1959.