

# The effects of periodontal treatment on diabetes

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**D**iabetes mellitus (type 1 and type 2) is a prevalent chronic disease of adults and children in the United States. Type 1 diabetes occurs predominantly in youth, although it can occur at any age. Type 2 diabetes is the most prevalent type of diabetes in the United States, affecting approximately 90 to 95 percent of people with diabetes. Although most people with diabetes who are older than 45 years of age have type 2 diabetes,<sup>1</sup> the prevalence of type 2 diabetes among adolescents is increasing at an alarming rate.<sup>2</sup>

Periodontal diseases, including gingivitis and severe periodontitis, are also common chronic infections in the U.S. population. More than 50 percent of U.S. adults have evidence of gingivitis, 35 percent have some form of periodontitis, and 7 to 15 percent have severe periodontitis.<sup>3,4</sup>

The characteristic metabolic disorder in diabetes is hyperglycemia, and when poorly controlled, it has been well-documented as the principal cause of the incidence and progression of microvascular complications (retinopathy, nephropathy and neuropathy) in people with diabetes. Results from several clinical trials have shown that intensive glycemic control can prevent or delay the onset and slow the progression of microvascular complications associated with both type 1 and type 2 diabetes.<sup>5,6</sup>

An extensive body of evidence supports diabetes as a risk factor in periodontal disease.<sup>7</sup> Also, indirect and direct evidence supports the concept that periodontal infection adversely affects glycemic control in people with diabetes. Indirect evidence supporting the biological plausibility of this link is derived from studies of the relationship between insulin resistance and the response to inflammation. Insulin resistance has been observed in active inflammatory connective tissue diseases,<sup>8,9</sup> other clinical diseases<sup>8-11</sup> and acute infection.<sup>12,13</sup> The inflamed periodontium is highly vascular, and

**Background.** Diabetes mellitus and periodontal diseases are common chronic diseases in the United States. Periodontal infection may adversely affect glycemic control in people with diabetes. This article reviews the evidence regarding how treatment of periodontal diseases affects glycemic control.

**Types of Studies Reviewed.** The review consisted of a MEDLINE literature search to identify primary research reports on the relationship between periodontal therapy and changes in glycemic control. The review identified three randomized clinical trials and nine nonrandomized clinical follow-up studies.

**Results.** The strength, quantity and breadth of evidence are varied, precluding clear-cut guidance for determining whether treating periodontal infection has a beneficial effect on glycemic control. Despite the variation and limitations in the literature, evidence supports the concept that periodontal diseases can contribute to poorer glycemic control in people with diabetes. Although the evidence is not unequivocal, it provides sufficient support for additional investigations of the effect of preventing and treating periodontal infections on managing glycemic control.

**Clinical Implications.** Sufficient evidence exists to incorporate oral examinations and periodontal care in management regimens for people with diabetes. It is prudent to assess patients' glycemic control status and communicate the importance of referring patients with diabetes for thorough oral health evaluations and necessary care.



the ulcerated pocket epithelium may serve as a portal to the systemic circulation for bacterial products and locally produced inflammatory mediators. Hence, chronic periodontitis, a predominantly gram-negative anaerobic infection, may serve as a focal source for sustained entry of bacterially derived lipopolysaccharides, or LPS, and host-produced inflammatory media-

**The evidence shows that periodontal diseases can contribute to poorer glycemic control in people with diabetes.**

tors into the systemic circulation.<sup>14,15</sup> Among the inflammatory mediators produced in response to the bacterial challenge responsible for chronic periodontitis are interleukin-1 beta, or IL-1 $\beta$ ; interleukin-6, or IL-6; and tumor necrosis factor-alpha, or TNF- $\alpha$ . These mediators have been shown to influence glucose and lipid metabolism. TNF- $\alpha$  has been reported to interfere with lipid metabolism and to cause insulin resistance.<sup>16-19</sup> IL-1 $\beta$  and IL-6 have been reported to antagonize insulin action.<sup>20-24</sup> Additionally, LPS has been shown to induce insulin resistance in rats.<sup>23,25</sup>

More direct evidence comes from a small number of clinical studies<sup>26-38</sup> that evaluated the effects of treating periodontal infection on glycemic control, and two epidemiologic studies<sup>39,40</sup> that assessed the detrimental effects of periodontal diseases on glycemic control. This article reviews evidence from clinical studies that assessed changes in glycemic control after periodontal therapy.

## METHODS

This literature review identified relevant studies using a comprehensive MEDLINE search of the post-1960 English language literature. The search sought primary research reports of relationships between periodontal therapy and changes in glycemic control in people with diabetes. The MEDLINE search was supplemented with inspection of the indexed articles' bibliographies to identify additional references.

The search also included inspection of reports and bibliographies of observational studies that provided information on the periodontal health of people with diabetes to locate additional studies in which people with diabetes were followed up after periodontal therapy. All of the reports reviewed included a minimum of subgingival scaling as part of periodontal therapy. The review encompassed a spectrum of periodontal diseases using the various definitions and classifications provided by the studies' authors (Table).

## RESULTS

The review identified three randomized clinical trials and nine nonrandomized clinical follow-up studies involving periodontal therapy in patients with diabetes in which changes in glycemic control could be assessed. The table summarizes these studies. Aldridge and colleagues<sup>26</sup> conducted two single-blinded clinical trials to study the effects of periodontal treatment on metabolic control in type 1 diabetes. The patients had satisfactorily con-

trolled type 1 diabetes at the time of enrollment in these studies. Periodontal treatment included scaling, root planing, selected extractions and oral hygiene instructions. Some patients in the second trial received extractions and endodontic therapy. The first trial included 31 participants (aged 16-40 years) with type 1 diabetes who had gingivitis and/or no attachment loss exceeding 2 millimeters; the second trial included 22 participants (aged 20-60 years) with type 1 diabetes who had evidence of advanced periodontitis. In both trials, the authors reported no improvement in metabolic control (as measured by a decrease in glycosylated hemoglobin, or HbA<sub>1c</sub>) two months after periodontal therapy.

The third randomized clinical trial, conducted by Grossi and colleagues,<sup>28</sup> assessed the efficacy of systemic doxycycline and topical antimicrobial irrigation accompanying ultrasonic bacterial curettage in the treatment of severe periodontitis associated with type 2 diabetes. All of the 113 participants (aged 25-65 years) had poorly controlled diabetes and severe periodontitis. Five treatment groups made up the study population; three groups received ultrasonic débridement and a combination of systemic doxycycline and irrigation with water, povidone-iodine or chlorhexidine. Two groups received ultrasonic scaling with either chlorhexidine or water irrigation and a placebo. The authors reported statistically significant (0.52-1 percent) reductions in the HbA<sub>1c</sub> concentration (that is, almost 5-10 percent of the pretreatment concentration) in the doxycycline-treated groups at the three-month assessment after periodontal therapy. The placebo groups had a smaller and nonsignificant diminution in HbA<sub>1c</sub>. This improvement accompanied a reduction in periodontal inflammation, as measured by gain in attachment level, and a reduction in periodontal infection, as measured by reduction in subgingival *Porphyromonas gingivalis*. After three months, the HbA<sub>1c</sub> levels increased, and at six months, all of the study groups exhibited HbA<sub>1c</sub> levels comparable to the baseline levels. However, the investigators did not provide further periodontal treatment after the initial treatment session. The authors proposed that the reduction in HbA<sub>1c</sub> in the groups treated with doxycycline may have been the result of doxycycline's antimicrobial effect, its modulation of host defenses and possibly its inhibition of the nonenzymatic glycosylation process.

Three nonrandomized clinical studies provide additional support for the beneficial effect of peri-

**TABLE**

EFFECTS OF TREATING PERIODONTAL DISEASE ON GLYCEMIC CONTROL: STUDY DESIGN FEATURES AND OUTCOMES.								
AUTHOR, YEAR	STUDY DESIGN	DIABETES TYPE	NO. OF SUBJECTS		BASELINE PERIODONTAL STATUS	PERIODONTAL THERAPY	METABOLIC CONTROL OUT-COME MEASURE	EFFECTS ON METABOLIC CONTROL
			Treatment (Age Range in Years)	Control (Age Range in Years)				
Aldridge et al: Study 1, 1995 <sup>26</sup>	RCT*	Type 1	16 (16-40)	15 (16-40)	Gingivitis, early periodontitis	OHI,† SRP,‡ adjustment of restoration margins and reinforcement after 1 month	Glycosylated hemoglobin, or HbA <sub>1c</sub> , fructosamine	No effect on change in HbA <sub>1c</sub>
Aldridge et al: Study 2, 1995 <sup>26</sup>	RCT	Type 1	12 (20-60)	10 (20-60)	Advanced periodontitis	OHI, SRP, extractions, endodontic therapy	HbA <sub>1c</sub>	No effect on change in HbA <sub>1c</sub>
Christgau et al, 1998 <sup>31</sup>	Treatment study, non-RCT	Type 1 and type 2	20 (30-66)	20 (30-67)	Moderate-to-advanced periodontitis	SRP, subgingival irrigation with chlorhexidine, OHI, extractions	HbA <sub>1c</sub>	No effect on HbA <sub>1c</sub>
Grossi et al, 1996, 1997 <sup>27,28</sup>	RCT	Type 2	89 (25-65)	24 (25-65)	Advanced periodontitis	Treatment groups received either systemic doxycycline or placebo and ultrasonic bactericidal curettage with irrigation using water, chlorhexidine or povidone-iodine	HbA <sub>1c</sub>	The three groups receiving doxycycline and ultrasonic bacterial curettage showed significant reductions ( $P \leq .04$ ) in mean HbA <sub>1c</sub> at 3 months
Iwamoto et al, 2001 <sup>37</sup>	Treatment study, non-RCT	Type 2	13 (19-65)	0	Gingivitis, chronic periodontitis	Mechanical débridement of plaque and local minocycline in each periodontal pocket once a week for 4 weeks	HbA <sub>1c</sub>	A significant improvement of HbA <sub>1c</sub> levels: significant reduction in circulating TNF- $\alpha$ § levels; significantly decreased fasting insulin levels and HOMA-R¶ in patients not receiving insulin

\* RCT: Randomized clinical trial.  
 † OHI: Oral hygiene instruction.  
 ‡ SRP: Scaling and root planing.  
 § TNF- $\alpha$ : Tumor necrosis factor-alpha.  
 ¶ HOMA-R: Homeostasis Model Assessment of Insulin Resistance.

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**TABLE (CONTINUED)**

EFFECTS OF TREATING PERIODONTAL DISEASE ON GLYCEMIC CONTROL: STUDY DESIGN FEATURES AND OUTCOMES.								
AUTHOR, YEAR	STUDY DESIGN	DIABETES TYPE	NO. OF SUBJECTS		BASELINE PERIODONTAL STATUS	PERIODONTAL THERAPY	METABOLIC CONTROL OUT-COME MEASURE	EFFECTS ON METABOLIC CONTROL
			Treatment (Age Range in Years)	Control (Age Range in Years)				
Miller et al, 1992 <sup>34</sup>	Treatment study, non-RCT*	Type 1	9 (not given)	0	Moderate-to-advanced periodontitis	SRP <sup>†</sup> , chlorhexidine rinses, systemic doxycycline	HbA <sub>1c</sub> , glycated albumin	Decrease in HbA <sub>1c</sub> and glycated albumin in patients with improvement in gingival inflammation ( <i>P</i> < .01)
Seppala et al, 1993, 1994 <sup>35,36</sup>	Treatment study, non-RCT	Type 1	38: 1 year; 22: 2 years <sup>‡</sup> 26 PIDD <sup>§</sup> : 1 year (48 ± SD <sup>¶</sup> 6) 12 CIDD <sup>#</sup> : 1 year (43 ± 5) 16 PIDD: 2 years 6 CIDD: 2 years	0	Chronic periodontitis	SRP, periodontal surgery and extractions	Medical history for baseline control status, HbA <sub>1c</sub> and blood glucose for assessing response to treatment	Reported an improvement of the HbA <sub>1c</sub> levels of the PIDD and CIDD subjects ( <i>P</i> < .068, <i>t</i> test)
Smith et al, 1996 <sup>29</sup>	Treatment study, non-RCT	Type 1	18 (26-57)	0	Advanced periodontitis	SRP with ultrasonics and curettes, OHI <sup>**</sup>	HbA <sub>1c</sub>	No statistically or clinically significant change in HbA <sub>1c</sub>
Stewart et al, 2001 <sup>38</sup>	Treatment study, non-RCT*, quasi-experimental design	Type 2	36 (62.4 ± SD <sup>†</sup> 8.4)	36 (67.3 ± SD 10.8)	Periodontitis	<b>Treatment group:</b> Full-mouth SRP <sup>†</sup> , subgingival curettage, OHI <sup>§</sup> , extraction of unsalvageable teeth with periapical radiolucencies and/or sufficient periodontal destruction <b>Control group:</b> Not treated by study team; medical records were reviewed for HbA <sub>1c</sub> measures only	HbA <sub>1c</sub>	Significant reductions in levels of HbA <sub>1c</sub> in treatment and control groups, 17.1% and 6.7%, respectively; difference in the changes between the two groups statistically significant ( <i>P</i> = .02)

\* RCT: Randomized clinical trial.  
 † SRP: Scaling and root planing.  
 ‡ Thirty-eight subjects were followed up for one year and 22 for two years.  
 § PIDD: Poorly controlled insulin-dependent diabetes.  
 ¶ SD: Standard deviation.  
 # CIDD: Controlled insulin-dependent diabetes.  
 \*\* OHI: Oral hygiene instruction.

**TABLE (CONTINUED)**

EFFECTS OF TREATING PERIODONTAL DISEASE ON GLYCEMIC CONTROL: STUDY DESIGN FEATURES AND OUTCOMES.								
AUTHOR, YEAR	STUDY DESIGN	DIABETES TYPE	NO. OF SUBJECTS		BASELINE PERIODONTAL STATUS	PERIODONTAL THERAPY	METABOLIC CONTROL OUT-COME MEASURE	EFFECTS ON METABOLIC CONTROL
			Treatment (Age Range in Years)	Control (Age Range in Years)				
Westfelt et al, 1996 <sup>30</sup>	Treatment study, non-RCT	Type 1 and type 2	20 (45-65)	20 (45-65)	Moderate periodontitis, advanced periodontitis	Baseline OHI, SRP followed by periodic prophylaxes, OHI, localized subgingival plaque removal, and surgery at sites with bleeding on probing and probing pocket depth > 5 millimeters	HbA <sub>1c</sub>	Mean HbA <sub>1c</sub> value between baseline and 24 months not significantly different from that between 24 and 60 months
Williams and Mahan, 1960 <sup>32</sup>	Descriptive clinical study	8 subjects with type 1; for 1 subject, type not specified	0.9 (20-32)	0	Gross evidence of periodontal disease	Extractions, scaling and curettage, gingivectomy, systemic antibiotics (intramuscular penicillin and streptomycin)	Insulin requirement, diabetes control (not operationally defined), blood glucose levels	7 of 9 subjects had significant reduction in insulin requirements and noticeable reduction in blood sugar levels
Wolf, 1977 <sup>33</sup>	Treatment study, non-RCT*	Type 1 and type 2	91 (16-60)	0	Gingivitis, moderate periodontitis	Scaling and intensive patient home care; periodontal surgery; extractions; endodontic treatment; restorations; denture replacement or repair	Blood glucose, 24-hour urinary glucose, insulin dose	Study compared 23 subjects who had improved oral infection with 23 who had no improvement after treatment for oral infection and inflammation; subjects with improved oral inflammation and infection tended to demonstrate improved control of diabetic symptoms ( $P < .1$ )

\* RCT: Randomized clinical trial.  
† SD: Standard deviation.  
‡ SRP: Scaling and root planing.  
§ OHI: Oral hygiene instruction.

odontal treatment with adjunctive antibiotic therapy on glycemic control in patients with diabetes.<sup>32,34,37</sup> Two reports included systemic antibiotics, and one included a locally delivered antibiotic with periodontal therapy. Williams and Mahan<sup>32</sup> reported that periodontal therapy led to reductions in insulin requirements and blood glucose levels for seven of nine patients at a U.S. Air Force hospital, who had “gross evidence of periodontal disease” during a follow-up period of at least three months. Eight of the nine patients had type 1 diabetes, and six of the nine were diagnosed with diabetes within the preceding seven months. One caveat to interpreting these results is that most patients with type 1 diabetes demonstrate a transient clinical remission phase early in the disease.<sup>41</sup> During this phase, lower doses of insulin may be required because of partial recovery of endogenous secretion of insulin, thus enhancing the ability to attain glycemic control.

Miller and colleagues<sup>34</sup> evaluated the effect of periodontal therapy in a pilot study of a group of nine dental school patients with poorly controlled type 1 diabetes and moderate-to-severe periodontitis. The patients were followed up for eight weeks. The mean HbA<sub>1c</sub> level decreased from 9.4 percent before treatment to 9.0 percent after treatment ( $P = .11$ ) for the nine patients. For the five patients exhibiting consistent improvement in periodontal bleeding response, the HbA<sub>1c</sub> level decreased from 8.7 percent pretreatment to 7.8 percent posttreatment ( $P < .01$ ). Patients who showed no improvement in bleeding had no improvement in HbA<sub>1c</sub>.

Iwamoto and colleagues<sup>37</sup> conducted a nonrandomized clinical study using antibiotics and evaluated the effect of periodontal treatment on circulating TNF- $\alpha$  levels, insulin resistance and HbA<sub>1c</sub> in 13 patients with type 2 diabetes and chronic periodontitis (12 patients) or gingivitis (one patient). After three months, they found a significant reduction in HbA<sub>1c</sub>, from a mean of 8.0 percent before treatment to 7.1 percent after treatment ( $P < .007$ ). This study also reported a significant reduction in serum TNF- $\alpha$ , fasting immunoreactive insulin (a measure of circulating endogenous insulin in patients who were not receiving insulin therapy) and a significantly reduced homeostasis model assessment index (an indicator of insulin resistance).

Three nonrandomized clinical studies in which antibiotics were not used suggest a beneficial effect of periodontal treatment on glycemic control. Wolf<sup>33</sup>

reported results of a study of periodontal treatment among 91 insulin-dependent patients with type 1 and type 2 diabetes. The report is limited to a comparison between 23 subjects whose oral infection improved and 23 subjects whose condition did not improve after treatment for oral infection and inflammation. Subjects with decreased oral inflammation and infection were more likely to have improved diabetes control (as measured by decreased urinary glucose levels, blood glucose levels and insulin dose) after eight to 12 months. Wolf considered the differences between the groups to be “statistically indicative” ( $P < .1$ ) of a beneficial effect.

Seppala and colleagues<sup>35,36</sup> conducted a two-year study of the periodontal condition of two groups of adults (aged 35 to 56 years) with type 1 diabetes after providing periodontal treatment. One group had poorly controlled type 1 diabetes ( $n = 26$  for one-year follow-up,  $n = 16$  for two-year follow-up) and the other had better-controlled diabetes ( $n = 12$  for one-year follow-up,  $n = 6$  for two-year follow-up). The first of two reports of this study<sup>35</sup> documented improved HbA<sub>1c</sub> levels in subjects with poorly controlled diabetes and in subjects with well-controlled diabetes during the two-year period, showing a reduction in mean HbA<sub>1c</sub> from baseline to two-year follow-up of 9.9 percent to 9.6 percent in those with poorly controlled diabetes and 9.5 percent to 7.6 percent in those with well-controlled diabetes ( $P < .068$ ). However, a second report<sup>36</sup> stated that the periodontal treatment did not significantly improve the HbA<sub>1c</sub> or blood glucose levels in the group with poorly controlled diabetes, while still reporting  $P < .068$ . Unfortunately, it was not possible to resolve the discrepancy in the results from the information provided.

Stewart and colleagues<sup>38</sup> studied changes in glycemic control associated with periodontal treatment in a group of 72 adults with type 2 diabetes and periodontitis. Baseline glycemic control ranged from good to poor for the patients ( $n = 36$  in the treatment group,  $n = 36$  in the comparison group). The medical records of the comparison group of randomly selected patients invited for treatment in the investigators’ dental clinic but who did not respond to the invitation were reviewed for HbA<sub>1c</sub> measures and other relevant information. However, the investigators reported that the dental status of the comparison group and the types of dental care received outside of the investigators’ clinic were not known. The authors reported statistically significant reductions in the levels of HbA<sub>1c</sub>

in both the treatment and comparison groups (17.1 percent and 6.7 percent, respectively). The mean time between the pretreatment and posttreatment HbA<sub>1c</sub> level measurement was 10 months. They also found the difference in the changes between the two groups to be statistically significant ( $P = .02$ ).

Three nonrandomized clinical studies reported that periodontal treatment had no beneficial effects on glycemic control. Smith and colleagues<sup>29</sup> studied the efficacy of nonsurgical periodontal therapy in 18 patients (aged 26-57 years) with advanced periodontitis and well-controlled type 1 diabetes. The investigators found no statistically or clinically significant change in the HbA<sub>1c</sub> level or insulin dose from baseline to the two-month follow-up visit.

Westfelt and colleagues<sup>30</sup> conducted a five-year longitudinal study to investigate differences in the ability of patients with and without diabetes who were treated for moderate-to-advanced periodontal disease to maintain a healthy periodontal status. Twenty patients with type 1 or type 2 diabetes and 20 controls without diabetes received nonsurgical periodontal therapy before the baseline examination that was performed three months later. Following the baseline examination, the investigators followed up the subjects every three months for five years, providing a professional plaque control program including tooth cleanings and surgical therapy in selected areas six months after the baseline examination. The investigators measured HbA<sub>1c</sub> at each examination and reported no significant difference in its mean value between the baseline-to-24-month and the 24-to-60-month intervals for the patients with diabetes.

Christgau and colleagues<sup>31</sup> compared the response to nonsurgical periodontal therapy in a group of adults with type 1 or type 2 diabetes (aged 30 to 66 years) who had moderate-to-advanced periodontitis. Twenty subjects had well-controlled diabetes (seven with type 1, 13 with type 2) and 20 control subjects did not have diabetes. The baseline level of glycemic control was good for 17 of the patients with diabetes and moderate or poor for three patients. The periodontal treatment consisted of two phases. The first phase provided patient motivation, oral hygiene instructions, supragingival scaling, emergency restorations, removal of overhanging margins, extractions of hopeless teeth and splinting of mobile teeth. The second phase provided nonsurgical periodontal therapy with subgingival scaling, root planing and

irrigation of all pockets with chlorhexidine. The investigators reported that, four months after the second phase of periodontal treatment, subjects with diabetes responded as well as did subjects without diabetes in demonstrating significant improvements in periodontal health. However, there was no significant change in HbA<sub>1c</sub> values at the four-month follow-up visit.

## CONCLUSION

This review of the literature on the effects of treating periodontal diseases on glycemic control shows the variation and limitations in the quantity, breadth and strength of evidence on this topic. Several factors influence the interpretations of the reports and limit the ability to form generalizable conclusions.<sup>15,42</sup> Perhaps the most striking limitation is the identification of only three published reports of randomized clinical trials.<sup>26-28</sup> This powerful experimental technique is recognized as the clearest method to determine the effectiveness of an intervention.<sup>43</sup> Other issues to consider in assessing the evidence include the following sources of heterogeneity among the studies reviewed:

- the type and number of diabetes-related factors studied (such as type of diabetes, baseline glycemic control status, diabetes duration, type of diabetes treatment);
- baseline periodontal disease status, periodontal treatment protocols and methods used to assess periodontal status;
- sample size and power to detect differences in periodontal and metabolic response;
- inclusion of control groups;
- follow-up time frame(s) for periodontal status and glycemic control evaluation;
- specific hypotheses tested.

Despite the variation and limitations, evidence supports the concept that periodontal diseases can contribute to poorer glycemic control in people with diabetes and that treating periodontal infections could have a beneficial effect on glycemic control in either type 1 or type 2 diabetes. The evidence is not unequivocal, but it is sufficient to support investigating the effects of preventing and treating periodontal infections as a way to contribute to glycemic control in people with diabetes, particularly using the multicenter, randomized clinical trial approach in diverse populations. Additionally, sufficient evidence exists for clinical practitioners to consider it prudent to incorporate a thorough oral examination and necessary periodontal care

(prevention and treatment) in management regimens for people with diabetes. Oral health care professionals should assess the glycemic control status of patients with diabetes by asking about their blood glucose self-monitoring practices and test results, as well as the date and results of their most recent HbA<sub>1c</sub> test and the frequency of HbA<sub>1c</sub> tests. It is also important to communicate with physicians and others involved in diabetes care about the importance of referring patients with diabetes for thorough oral health evaluations and necessary oral health care. ■

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