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The Relationship between Smoking and Acute Necrotizing Ulcerative Gingivitis (ANUG): A Scoping Review

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Abstract

Smoking is a serious public health problem. The condition of the oral cavity is directly affected by smoking, and this is associated with an increase in calculus formation resulting in an increased risk of periodontal disorders. Acute necrotizing ulcerative gingivitis (ANUG) is one of the periodontal disorders caused by the presence of bacteria or microbes in the gingival region. However, it can also be affected by risk factors including smoking which can cause various periodontal tissue changes. The purpose of this review is to determine the relationship and characteristics of acute necrotizing ulcerative gingivitis (ANUG) related to smoking. This review is a literature review using the scoping review method. This method facilitated the collection of relevant studies with different methodologies and examination to clarify the definition of a topic and map the conceptual boundaries of a topic. Articles were searched using PubMed, Science Direct, Wiley, and Scopus databases from November 2023 to January 2024 with inclusion criteria of English language articles discussing ANUG with risk factors for tobacco smoking. The study design used in the articles consisted of 5 articles with cross-sectional studies and 3 articles with case-control studies. This review looked at the effect of smoking on ANUG based on smoking status and amount, clinical signs, and treatment. Seven of the eight articles reviewed stated that there was a significant association between smoking and ANUG. Smoking has a significant association with acute necrotizing ulcerative gingivitis (ANUG) by affecting the condition of periodontal tissues.

Keywords: Acute necrotizing ulcerative gingivitis; ANUG; smoking habit; smoker.

INTRODUCTION

Today, smoking is a serious public health problem. The effects are very harmful to the human body. The condition of the oral cavity is directly affected by the habit of smoking, and this habit is associated with an increase in the formation of calculus so that the risk of periodontal abnormalities increases. Several studies have shown that smoking is a risk factor in the etiology of periodontal disease, with both local and systemic effects (Leite et al., 2018; Nazir, 2017). Recent studies on smoking habits have also shown a greater prevalence of attachment loss, recession, severe destructive periodontal disease, and poor response to non-surgical or surgical periodontal care in groups of smokers, compared to non-smokers. Smoking habits will affect the blood supply to periodontal tissue (Silva, 2021). In some studies of plaque-induced gingivitis, it was stated that clinical signs were reduced and the tendency of gingival bleeding was less due to the presence of vascular changes caused by smoking.

Tar in smoke has a direct irritating effect on the gingival causing gingivitis and nicotine can cause vasoconstriction of gingival in the peripheral circulation, thereby disrupting adequate gingival nutrition, consequently reducing the resistance of the host's immunity to infection (Alayadi, 2024; Kravchenko & Lykhota, 2024). If blood flow to the gingival margin is already disrupted due to inflammation, stress, poor diet or cold weather, nicotine can disrupt further flow, causing "aseptic necrosis".Patients treated for ANUG's disease are often accompanied by smoking habits. Clinical and epidemiological studies also state that most cases of refractory periodontal conditions occur in smokers and have a dose-dependent relationship, meaning that the greater the number of cigarettes smoked and the longer the smoking habit, the greater the damage to the periodontal tissue.

Acute Necrotizing Ulcerative Gingivitis (ANUG) is caused by the presence of bacteria or microbes in the gingival region, destroys quickly (destructive) and most often occurs in a person with a compromised immune system (Aaron & DeBlois, 2023). This can be accompanied by systemic symptoms. *Acute Necrotizing Ulcerative Gingivitis* (ANUG) has been recorded and known for hundreds of years by various names.(Aaron & DeBlois, 2023; Prince, 2012) The incidence of ANUG varied over time, with very high rates recorded among the military population during World Wars I and II (Neville et al., 2019). The disease affects <1% of the population (Aaron & DeBlois, 2023; Dufty, Gkranias, & Donos, 2017). ANUG disease should not be underestimated despite its low prevalence as it is one of the most severe responses to oral biofilm and is one of the emergencies in periodontals.(Dufty, Gkranias, & Donos, 2017) An accurate picture of the prevalence and severity of ANUG is difficult to determine due to changes in nomenclature or terms over time.(Dufty, Gkranias, Petrie, et al., 2017) The diagnosis of ANUG can generally be determined on the clinical signs found, due to the sufficiency of the typical characteristics that distinguish this disease from others. This is supported by researchers who found that organisms associated with this disease may be present in the mouths of periodontally healthy individuals. Although ANUG has been identified sufficiently through clinical findings, there is still much that is not understood about the etiology and pathogenesis of ANUG related to its risk factors, one of which is smoking habits (Gollapudi et al., 2024; Kwon et al., 2016; Rustgi et al., 2021).

Despite these valuable contributions, significant research gaps remain. First, most previous studies have focused on specific populations (military personnel, dental school patients, adolescents) with limited generalizability. Second, there is no recent systematic synthesis of evidence specifically examining the relationship between smoking and ANUG using a scoping review methodology that maps both clinical and biological mechanisms. Third, the dose-response relationship between smoking intensity (cigarettes per day, pack-years, duration) and ANUG severity has not been comprehensively reviewed. Fourth, the specific clinical characteristics of ANUG in smokers versus non-smokers require further elucidation. The urgency of this research is underscored by: (1) the high global prevalence of smoking (1.3 billion users); (2) the potential for misdiagnosis of ANUG due to overlapping clinical features with other periodontal conditions; (3) the need for evidence-based smoking cessation interventions as part of ANUG treatment protocols; (4) the emergence of new tobacco products (e-cigarettes, heated tobacco) that may have similar or different effects on periodontal health.

Based on the description above, smoking habits are one of the factors in the occurrence of ANUG disease, so the relationship and characteristics must be clarified to determine the influence of smoking habits on ANUG disease because of the many occurrences of ANUG in individuals who have a smoking habit. This study was conducted with the aim of determining the relationship and characteristics of *acute necrotizing ulcerative gingivitis* (ANUG) related to smoking habits.

RESEARCH METHODS

This research was a *literature review*. The methodology used in this study was *scoping review*. This method can facilitate the collection of various studies/literature relevant to different methodologies and examinations to clarify the definition of a topic and map the conceptual boundaries of a topic.(Mozgai et al., 2023; Watkins et al., 2023) This method is

very useful for finding and synthesizing research where the field of research is still developing or the evidence on a topic is still unclear.(Ryan et al., 2023) The tools and materials used during the study were office stationery (ATK), electronic devices (laptops and mobile phones), search engines *database* (PubMed, Science Direct, Wiley, dan Scopus), *software* Microsoft, and Mendeley.

The article search was conducted from November 2023 to January 2024 online at the author's domicile. The inclusion criteria in this study are articles that discuss ANUG with risk factors for tobacco smoking, articles in English, articles with observational study research designs (*cohort study, cross-sectional study, and case-control study*), *case reports*, and *clinical studies*, as well as *full-text* articles that are accessible and meet the research keywords. The exclusion criteria in this study are articles that discuss periodontal diseases other than ANUG such as ANUP, periodontal abscess, periodontitis, dental material materials, and dental practice management, articles related to *necrotizing* accompanied by bone loss, articles with research *design literature reviews, conference papers,* and *posters*.

The article search process is carried out on *database* using terminology and keyword combinations in *Boolean Operator*, is ("Acute Necrotizing Ulcerative Gingivitis" OR "ANUG") AND ("Smoker" OR "Smoking Habit").(Ryan et al., 2023; Tan et al., 2023) Furthermore, a study selection was carried out with a PRISMA-ScR (Preferred Reporting Items for Systematic Reviews and Meta-Analyses for Scoping Review) checklist as a guide to select articles that are in accordance with the topic and research objectives with the process of identifying research questions using the PCC (population, concept, and context) model to facilitate the article search process.(Ryan et al., 2023; Tan et al., 2023) The PCC criteria used in the study were: 1) Population: individuals who smoke with ANUG disease; 2) Concept: the relationship and characteristics of ANUG in individuals with smoking habits; 3) Context: individuals who have a habit of smoking tobacco with/without the presence of systemic disorders.

The article search process is carried out in several stages. The first stage, article search on PubMed, Science Direct, Wiley, Scopus databases. Articles obtained from searches are deleted duplicate articles.(Ryan et al., 2023) After that, titles and abstracts that are not relevant according to the inclusion and exclusion criteria are also removed. Finally, the article is checked through *full-text* for its eligibility. Thus, articles that have gone through the selection process will be selected for review by the *scoping review*.(Tan et al., 2023)

The novelty (novelty) of this research lies in several aspects. First, this is a scoping review that systematically maps the existing evidence on the smoking-ANUG relationship using the PRISMA-ScR framework, which is more comprehensive than traditional narrative reviews. Second, this review synthesizes evidence across multiple dimensions: epidemiological (prevalence, odds ratios), clinical (signs, symptoms, attachment loss), biological (vascular, immunological, microbiological mechanisms), and therapeutic (treatment outcomes, smoking cessation). Third, this review identifies research gaps and provides directions for future studies. The purpose of this research is to determine the relationship and characteristics of acute necrotizing ulcerative gingivitis (ANUG) related to smoking habits. The theoretical benefit of this research is to contribute to the body of knowledge on periodontal disease etiology and the role of modifiable risk factors. The practical benefits include: (a) providing evidence-based information for dental practitioners on the importance of smoking

cessation in ANUG management; (b) informing public health policies on tobacco control and oral health; (c) guiding future research directions on the mechanisms linking smoking and periodontal necrosis. The broader implication is the reduction of ANUG incidence and severity through targeted smoking cessation interventions.

RESULTS AND DISCUSSION

595 articles were generated from searches using the PubMed, Wiley, ScienceDirect, and Scopus databases with details of 43 articles obtained from the PubMed Database, 334 articles from the Wiley Database, 111 articles from the ScienceDirect Database, and 107 articles from the Scopus Database. The total number of articles identified was 595. A total of 319 articles were eliminated after article selection based on the type of research and left 276 articles for duplication checks. 24 articles were eliminated after a duplicate check and 252 articles remained. A total of 228 articles were eliminated after article selection based on titles and abstracts. The remaining twenty-four (24) articles were selected based on eligibility criteria. Sixteen (16) articles were excluded because they did not meet the inclusion criteria and were irrelevant, leaving 8 articles to be reviewed using the *scoping review method* in this study. The results of the article selection for the research are illustrated in the PRISMA-ScR diagram shown in the Chart below.

Eight articles were selected using various observational study and *case-report* designs, namely 4 articles using *cross-sectional* study designs, 2 articles using *case-control* study designs, and 2 articles using *case-report* study designs. The results showed that six out of eight articles studied stated that there was a positive association between smoking habits and *acute necrotizing ulcerative gingivitis* (ANUG). The remaining two articles state that smoking habits are not related to ANUG, either when considered together with the duration of smoking and when considered together with the number of cigarettes smoked. This may be because smoking exposure in the study population was too low to be able to clearly show the impact of smoking.

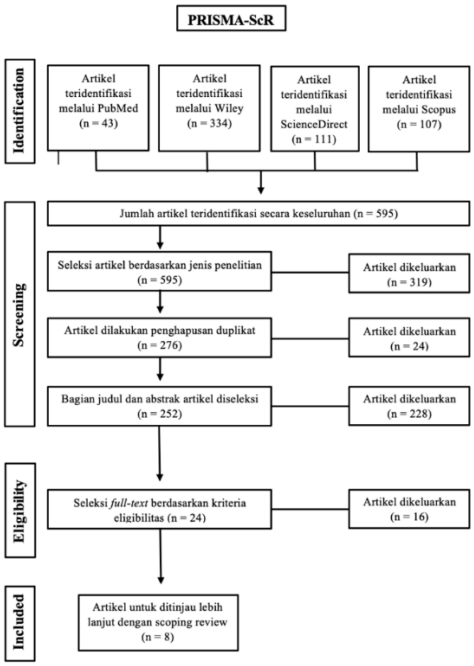

Image 1. Alur PRISMA-ScR

The presented studies focused on the prevalence, risk factors, and clinical features of Acute Necrotic Ulcerative Gingivitis (ANUG) in a variety of populations, with a significant emphasis on smoking as a causative factor. Dufty et al. (2017) found the prevalence of ANUG in the British Armed Forces to be 0.11%, with a strong association with smoking and poor oral hygiene. López and Bælum (2004) reported an association between ANUG lesions and loss of clinical attachment in high school students in Santiago, Chile. In their study, MacCarthy and Claffey (1991) observed greater loss of clinical attachment in ANUG patients compared to other periodontal conditions. Falkler et al. (1987) found clinical symptoms such as fetid bad breath and *pseudomembrane* formation to be common in ANUG patients, especially in those who smoke. Stevens et al. (1984) noted that most ANUG patients were under 25 years of age, with most being smokers. López et al. (2002) reported a prevalence of ANUG of 6.7% among adolescents, with diabetes having a significant association with an increased incidence of ANUG. A case report by Sheng et al. (2022) highlights how malnutrition, along with smoking, exacerbates necrotic periodontal disease. Finally, Chaubal and Bapat (2017) emphasized stress and smoking as the main predisposing factors of ANUG in their case study, suggesting proper diagnosis and lifestyle management for treatment. Overall, these studies emphasize the importance of oral hygiene, smoking cessation, and early detection in the prevention and management of ANUG.

Various studies on Acute Necrotic Ulcerative Gingivitis (ANUG) have identified risk factors, clinical symptoms, and treatment options in different populations. Dufty et al. (2017) reported that the prevalence of ANUG in the British Armed Forces ranged from 18 to 52 years of age, with smoking as a major factor. The treatment received by patients included OHI, *debridemen*, antibiotics, and mouthwash, but smoking cessation was only given in 6.8% of cases. López and Bælum (2004) found an association between smoking and ANUG lesions in adolescents in Santiago, Chile, although the treatment for ANUG is not described. MacCarthy and Claffey (1991) reported an association between ANUG and increased clinical attachment in patients aged 18 to 27 years, with the majority of patients smoking, and they received OHI and scaling treatments. Falkler et al. (1987) noted that 83% of ANUG patients in the Maryland clinic were smokers, with symptoms such as ulceration and interproximal papilla necrosis. Stevens et al. (1984) also found that 94% of ANUG patients were smokers, with treatment including scaling, gingival debridement, and OHI. López et al. (2002) observed that smoking was not a significant predictor for ANUG, but they reported the prevalence of necrotic ulceration lesions in adolescents. Sheng et al. (2022) noted severe inflammation of the gingiva and necrosis of the interdental papillae in a 22-year-old patient who smoked heavily, with treatment including debridement, analgesics, antibiotics, and behavioral education. Finally, Chaubal and Bapat (2017) described cases of heavy smokers with gingival necrosis, *pseudomembranes*, and increased body temperature, who also received debridement treatment and diet education and smoking cessation. Overall, these studies demonstrate the importance of early detection and lifestyle management in the prevention and treatment of ANUG, particularly among smokers.

Discussion

The habit of smoking is something that is often found in people that has bad effects on health, one of which is the health of the oral cavity (Sarumathi et al., 2019). Smoking interferes with the body's inflammatory response and immune system by activating endothelial and

inflammatory cells to induce cytokine secretion. Cigarettes have a damaging effect on periodontals, namely changes in the blood vessels of periodontal tissue, direct alternative effects on bacterial microflora, and inhibitory effects on immunoglobulin levels and antibody responses to plaque bacteria (Mishra & Mishra, 2013). The occurrence of plaque accumulation with tar deposits and tissue ischemia due to vasoconstriction by nicotine substances, this can increase the development of ANUG. The nicotine substance in cigarettes has a vasoconstricting effect on the blood vessels at the end of the gingival artery so that gingival hemorrhage in smokers is less severe when compared to those who do not smoke. Smoking regulates increased expression of pro-inflammatory cytokines, such as interleukin-1, which contributes to increased tissue damage and alveolar bone resorption (Mishra & Mishra, 2013; Sarumathi et al., 2019). Tobacco components can have a damaging effect on the function of neutrophils, namely the function of chemotaxis/phagocytosis or both. Smoking can also increase bacterial adhesion to epithelial cells and have a differential effect on bacterial colonization, which favors the growth of Gram-negative bacteria. Periodontal pocket oxygen pressure (PO2) was significantly lower in smokers compared to non-smokers (Mishra & Mishra, 2013).

Therefore, smokers are more likely to experience periodontal damage than non-smokers. A positive correlation was found between serum levels of nicotine metabolite cotinine and the severity of clinical attachment loss (CAL), probing depth, and alveolar peak height, where smoking significantly increased the risk of tooth loss by 70%.

The results of the review of the articles that have been carried out show that there is a relationship between *acute necrotizing ulcerative gingivitis* (ANUG) and smoking habits in the age range of 12-52 years. Research conducted by (Dufty, Gkranias, Petrie, et al., 2017), Stevens et al (1984), MacCarthy and Claffey (1991), and Falkler et al. (1987) stated that the research population is in the average age range of 23-24 years, which is in line with other studies that state that ANUG is a disease that is mainly suffered by young adults. In the study of Melnick S et al, it was shown that the average age of onset of ANUG was 23 years. In research Stevens et al (1984) and Falkler et al. (1987), the majority of ANUG patients are under 25 years old, which is more than 50%. ANUG does not appear to occur before the age of mid-teens, this statement is in line with research López et al. (2002) which shows students aged 18-20 years are 1.4 times more likely to have ANUG than students aged 12-14.

Two out of three articles stated that ANUG was more likely to occur in women than men. Another article shows a slightly higher percentage of men than women. However, this percentage difference with the general clinical population is not statistically significant.

From previous research evidence, it is known that smoking has a strong relationship with ANUG. Seven of the eight articles stated that smoking habits affect the chances of ANUG, both smoking status and the number of smokers (Dufty, Gkranias, Petrie, et al., 2017). In research Dufty et al, (2027) he pointed out that when the number of cigarettes smoked increased by one stick/day, the chances of becoming ANUG increased by about 19%. Instead, research conducted by López et al. (2002) showing smoking habits is not an important predictor and is not related to ANUG, both from the duration of smoking and the number of cigarettes. This may be the case because in this study population based on age range, the average duration of smoking among smokers was relatively short (less than 3 years) and the average number of cigarettes smoked was also quite low (5 cigarettes/day) so that smoking exposure in this young population was too low to be able to show the impact of smoking. Research conducted by

Stevens et al, (1984) states that not all patients with ANUG smoke and a large number of smoking controls so smoking is not considered a major diagnostic factor or etiological factor but rather one of the predisposing or causative factors. Falkler et al. (1987) in line with the concept Stevens et al. (1984) The onset and development of ANUG is characterized by a unique interaction of several physiological, psychological, immunological, and microbiological etiological factors.

ANUG is associated with loss of attachment, although it is generally considered to be gingivitis. However, clinical experience shows that loss of periodontal attachment is one of the consequences of this disease. This is proven in research MacCarthy and Claffey (1991) and López and Bælum which indicates that there is greater clinical attachment loss in the periodontal affected ANUG than in other areas. In addition, López and Bælum (2004) shows that the greater the number of cigarettes smoked, the greater the chance of ANUG with loss of clinical attachment (CAL), especially CAL 1 and CAL 3.

Loss of clinical attachment (CAL) has been associated with ANUG, but not with pocket depth. Dufty et al, (2017) shows a strong link shown between ANUG and current smokers and cases with *score basic periodontal examination* (BPE) overall 3. Analysis of risk factors against the control group showed that the chance of ANUG was 7.3 times greater for subjects with a BPE score of 3 compared to those with a BPE score of 0. A BPE score of 3 indicates a probing depth of 3.5 - 5.5 mm and indicates a pocket depth of 4-5 mm according to the British Society of Periodontology (BSP) guidelines. The BSP states that if a score of 3 occurs, then full 6-point pocket mapping should be performed on the sextant and most likely requires oral hygiene instruction (OHI) and root surface debridement.

In research Pindborg, (1947) calculus deposition is comparable to tobacco consumption where the greater the amount of tobacco smoked, the higher the chance of developing calculus both *supragingival* and *subgingiv*. There is an increase in calculus deposits in smokers due to the possibility of retention caused by *stain* tobacco. The study shows the more a person smokes, the greater the chance of developing ANUG and calculus buildup.

Some researchers have reported that fever is a characteristic finding in ANUG. In research Stevens et al, fever is an uncommon sign with only 20% coming in with temperatures greater than 98.6°F and no control patients coming in with high temperatures (>98.6°F). Nicotine can result in tissue ischemia so that the resistance of the host (gingiva) is reduced. This fact may be supported by ANUG patients who showed a lower average oral temperature than the control group. Unlike research Stevens et al and Wilson et al, The ANUG group tended to have a lower average body temperature compared to the control group in the study Shields. This suggests that a high body temperature is not a diagnostic sign for ANUG. Goldhaber & Giddon (1964) stated that an increase in temperature should indicate the presence of some disease other than ANUG. Research results Stevens et al. (1984) This hypothesis reinforces and suggests that conflicting reports of increased temperature in ANUG are due to confusion in diagnosis, not differences in symptoms. Thus, there is a high probability that ANUG patients experience a slight decrease in temperature as well as a large increase in temperature. These inconsistent temperatures result from ANUG that provoke an inflammatory response, other factors that may alter this process so that this sign is unreliable.

Falkler et al. (1987) states that in order for the clinical condition to be diagnosed as ANUG, the patient must experience ulceration and necrosis of the interproximal papillary, pain

and bleeding. Patients in this study showed this characteristic by 100%. However, there are other factors related to ANUG that are also evaluated. These factors are bad odor, *pseudomembrane* formation, lymphadenopathy, and increased temperature.

In a study conducted by Dufty et al. (2017), a two-way analysis of the type of treatment is performed to examine the relationship between the various treatments given. The results showed a significant association between treatments, i.e. if the case received OHI, he or she was more likely to receive debridement or antibiotics or smoking cessation advice, and if the case received *debridement,* he was more likely to receive antibiotics than not to receive antibiotics. Cases that received more than 2 types of treatment were 48.2% (92). Cases that received 3 types of treatment were 34.5% (66). Cases that received 4 types of treatment were 12.1% (23), and cases that received 5 types of treatment were 1.6% (3). The majority of subjects received oral hygiene instructions (and/or) were prescribed antibiotics or mouthwashes. Almost half (48.7%) received debridement, with only a small fraction prescribed analgesics or advised to quit smoking. There is a relationship between poor oral health and ANUG, it is hoped that there will be more evidence or facts related to the acceptance of oral hygiene instruction treatment. Therefore, the cases of ANUG who received oral hygiene instructions in this study appeared to be low, which was only 66.5%. A total of 2/3 of the total patients receive antibiotics. To increase the healing time of ANUG, additional treatment of mouthwash can be used until the patient can brush his teeth properly because brushing the teeth on the area with open wounds can delay the healing process and feel pain. Debridement has been recommended by several researchers and should be performed at the initial stage of ANUG's treatment. In research Dufty et al. (2017), analgesics are only prescribed in 8.4% of cases, this seems very low given the potential pain severity that can occur in ANUG. Antibiotics take time to take effect, and the debilitating nature of pain is so it is recommended that more patients receive analgesics in addition to antibiotics. In research MacCarthy and Claffey, each patient has also received oral hygiene instruction (OHI) treatments, *debridemen,* and systemic antimicrobial therapy.

Based on the explanation that has been explained above, it is known that smoking habits have a significant influence on *acute necrotizing ulcerative gingivitis* (ANUG) through various mechanisms of changes in the condition of periodontal tissue, namely clinically and biologically. Clinically, it is seen in loss of clinical adhesion, increased pocket depth, ulceration and necrosis of interproximal papillae, gingival hemorrhage, and *pseudomembrane* formation. Biologically, there is an increase in the number of bacteria so that the number of plaques and calculus increases which, in turn, can produce bad breath, as well as constriction of the gingival blood vessels. In addition, the greater the amount of smoking smoked, the greater the chance of ANUG. High body temperature is not a diagnostic sign for ANUG because there is a high chance that ANUG patients will experience a slight decrease in temperature or an increase in temperature. ANUG treatment is given more than one type of treatment according to the patient's condition, namely oral hygiene instructions, *debridemen*, antibiotics, analgesics, mouthwash, and smoking cessation. For ANUG patients who have a smoking habit, additional treatment must be given in the form of smoking cessation because smoking can play a role in the development of ANUG so that smoking during ANUG treatment must be stopped.

CONCLUSION

There is a relationship between smoking habits and acute necrotizing ulcerative gingivitis (ANUG) by modifying the condition of periodontal tissue. This is based on clinical findings in smokers with ANUG that show several changes in periodontal tissue such as loss of clinical attachment, increased pocket depth, ulceration and necrosis of interproximal papillae, gingival hemorrhage, and *pseudomembrane* formation, as well as biological changes that indicate an increase in the number of bacteria, plaque and calculus.

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