Prevalence of cervical squamous intraepithelial lesion high grade according to age from Antônio Pedro University Hospital

Prevalência de lesão intraepitelial escamosa de alto grau do colo uterino de acordo com a faixa etária no Hospital Universitário Antônio Pedro

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ABSTRACT

Introduction: The targeted population for HPV infection has peak infection at young adults, but studies point to the emergence of a new peak of viral infection and injuries later, probably by changes in sexual behaviour, waning immunity over time or reactivation of latent infection. Whereas the cervical squamous intraepithelial lesion high grade, mainly cervical intraepithelial neoplasia grades III (CIN III) have significant potential for progression to invasive carcinoma, the procedures of choice for the diagnosis and treatment in the target population are essential for the prevention of cervix cancer. **Objective:** To determine the prevalence of CIN II/III among patients seen in Cervical Pathology Clinic of Gynecology Department at the University Hospital Antonio Pedro from May 1996 to May 2013, relating to age in which this diagnosis was made. **Method:** It was selected patients referred to the Cervical Pathology Clinic for altered cytology and diagnosed through biopsy guided by colposcopy with CIN II / III. They were segmented into the following age groups: 15 to 24, 25 to 34, 35 to 44, 45 to 54, 55 to 64, 65 to 74, 75 to 84 and 85 to 94 years old. **Results:** Between 25 and 64 years of age, there were 36.5% of patients in these age groups with CIN II/III. However, it was found that 19% of patients younger than 25 years and 14.2% at 64 years also had such a diagnosis. **Conclusion:** The target population according to Brazilian Ministry of Health would let 16.2% of women with high-grade lesions withouta diagnosis, which corresponds to 11.3% of all high-grade cervical lesions.
Keywords: Human papillomavirus 16; Human papillomavirus 18; cervical intraepithelial neoplasia; age groups; statistics & numerical data.

RESUMO

Introdução: A população alvo de infecções pelo HPV tem como pico adultos jovens, porém estudos apontam para um novo pico mais tardio, provavelmente por alterações do comportamento sexual, diminuição da imunidade ou reativação da infecção latente. Considerando que as lesões intraepiteliais escamosas de alto grau do colo uterino, sobretudo a neoplasia intraepitelial cervical grau III (NIC III) tem potencial significativo de progressão para carcinoma invasor, os procedimentos de escolha para diagnóstico e tratamento na populaçãoalvo são essenciais para a prevenção do câncer de colo uterino. **Objetivo:** Verificar a prevalência de NIC II/III dentre as pacientes atendidas no Ambulatório de Patologia Cervical do Serviço de Ginecologia do Hospital Universitário Antônio Pedro no período de maio de 1996 a maio de 2013, relacionando com a faixa etária em que este diagnóstico foi realizado. **Método:** Selecionou-se as pacientes encaminhadas ao Ambulatório de Patologia Cervical por citologia oncótica alterada e diagnosticadas, por meio de biópsia dirigida pela colposcopia, com NIC II/III. Foram segmentadas nas seguintes faixas etárias: 15 a 24, 25 a 34, 35 a 44, 45 a 54, 55 a 64, 65 a 74, 75 a 84 e 85 a 94 anos. **Resultados:** Entre 25 e 64 anos de idade, houve 36,5% de pacientes nestas faixas etárias com NIC II/III. Entretanto, verificou-se que 19% de pacientes com menos de 25 anos e 14,2% com mais de 64 anos também apresentavam tal diagnóstico. **Conclusão:** A população-alvo preconizada pelo Ministério da Saúde deixaria 16,2% das mulheres com lesões de alto grau à margem de um diagnóstico, o que corresponde a 11,3% de todas as lesões de alto grau do colo uterino.
Palavras-chave: Papillomavirus Humano 16; Papillomavirus Humano 18; neoplasia intraepitelial cervical; grupos etários; estatística & dados numéricos.

INTRODUCTION

Infection by the human papillomavirus (HPV) has become a pandemic, which has attracted the attention of health-care professionals. HPV is classified, according to oncogenic potential, as having low and high risk. Among the various types of oncogenics, HPV16 and HPV18 can be pointed out, as they are able to integrate themselves into the genome of the host and block cellular mechanisms that control proliferation and repair deoxyribonucleic acid[1-3].

HPV is transmitted through sexual intercourse. From this moment on, the infection can become latent, which is diagnosable only through molecular biology; subclinical, which is diagnosable through colposcopy and cytology; or clinical, viewed through the naked eye. However, the majority of infections behave in a transitory form. Persistent infection with HPV constitutes biggest risk factor for the occurrence of lesions[2,3].

The precursor lesions were screened for cervical cancer in three distinct forms, depending on the guidelines for each country: only by cytopathology, such as in Brazil; only with the HPV test; or through a combination of both cytopathology and HPV test. According to the guidelines from the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology[4], the screening is performed in the following manner: women younger than 21 should not be screened, women aged between 21 and 29 should be screened only by cytology every

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3 years, and women aged between 30 and 65 should be screened preferably with cytology and the HPV test (co-test) every 5 years. Women more than 65 years of age with prior negative screening and no history of CIN 2 in the last 20 years should not be screened, whereas those more than 65 years of age with a history of CIN 2, CIN 3, or adenocarcinoma *in situ*, after either spontaneous remission or treatment, should continue the screening for at least 20 years after detection, even if they have surpassed the age of 65. For the confirmation, a colposcopy examination is performed[5,6].

When analyzing the natural history of CIN, CIN 2 is found to progress into CIN 3 in 22% cases and into invasion in 5% cases. Meanwhile, the progression rate of CIN 3 into invasion was more than 12%[7-9].

To treat the high-grade lesions of the cervix and, by consequence, prevent an invasive carcinoma, the recommended procedures are classic conization and large-loop excision of the transformation zone of the cervix[10].

OBJECTIVE

To analyze the cases of histopathological diagnosis of CIN 2 and 3 attending the Cervical Pathology Clinic at the Gynecology Department of the Antonio Pedro University Hospital, from May 1996 to May 2013, relating them to the age group of the patients.

MATERIALS AND METHODS

This was a retrospective study in which subjects were the patients referred to the Cervical Pathology Clinic at the Gynecology Department of the Antonio Pedro University Hospital for altered oncotic cytology, that is, atypical squamous cells of undetermined significance (ASC-US)[11] and diagnosed, through a biopsy by colposcopy, with high-grade cervical squamous intraepithelial lesion (CIN 2 and 3). The age group in which the diagnosis occurred was analyzed. The patients were divided into the following 10-year age groups: 15–24 years, 25–34 years, 35–44 years, 45–54 years, 55–64 years, 65–74 years, 75–84 years, and 85–94 years, in accordance to what was presented in a similar American study[12]. Women with a histopathological diagnosis of CIN 2 or 3 were included in the study.

RESULTS

From the 1,084 patients with altered cytology results in the 17 years of the retrospective study, 347 presented CIN 2 or 3 (**Table 1** and **Graph 1**).

When considering the altered cytology in the age group according to the Brazilian Ministry of Health (25–64 years), we had a total of 36.5% patients with high-grade lesions (CIN 2 or 3). However, 19% patients aged less than 25 years and 14.2% more than 64 years also presented the said histopathological diagnosis. Therefore, when the patients under 25-year and over 64-year age group were combined, 16.2% were found to be with CIN 2 or 3 (**Graph 2**).

When compared to the women in the age groups 21–24 years and 65–74 years, 23.5 and 16.3% patients were found to present high-grade lesions, respectively. Then, on adding the patients from these two age groups, 19.4% were found to be with CIN 2 or 3 (**Graph 3**).

From the 347 patients with histopathological diagnosis of CIN 2 or 3, we can determine the total number of women affected according to the age group (**Graph 4**).

It was found that 5.5% of women under 25 years and 5.8% over 64 years had high-grade cervical intraepithelial lesions. Thus, when combined, the patients from these two age groups, 11.3% were found to have CIN 2 or 3 (**Graph 5**).

Of the 347 patients with CIN 2 or 3, those aged between 21 and 24 and between 65 and 74 represented, respectively, 4.6% and 4.3% of total high-grade lesions, which corresponds to 8.9% cases with CIN 2 and 3.

DISCUSSION

This paper aimed at demonstrating the importance of a broader target population for the screening of cervical cancer, so that the lowest possible number of patients with CIN 2 or 3 can occur and, thus, provide epidemiologic impact on the reduction of new cases of cervical cancer. For this, it was necessary to analyze the age of the patients with precursor lesions and reflect on the need for changes in the age groups that were screened in Brazil.

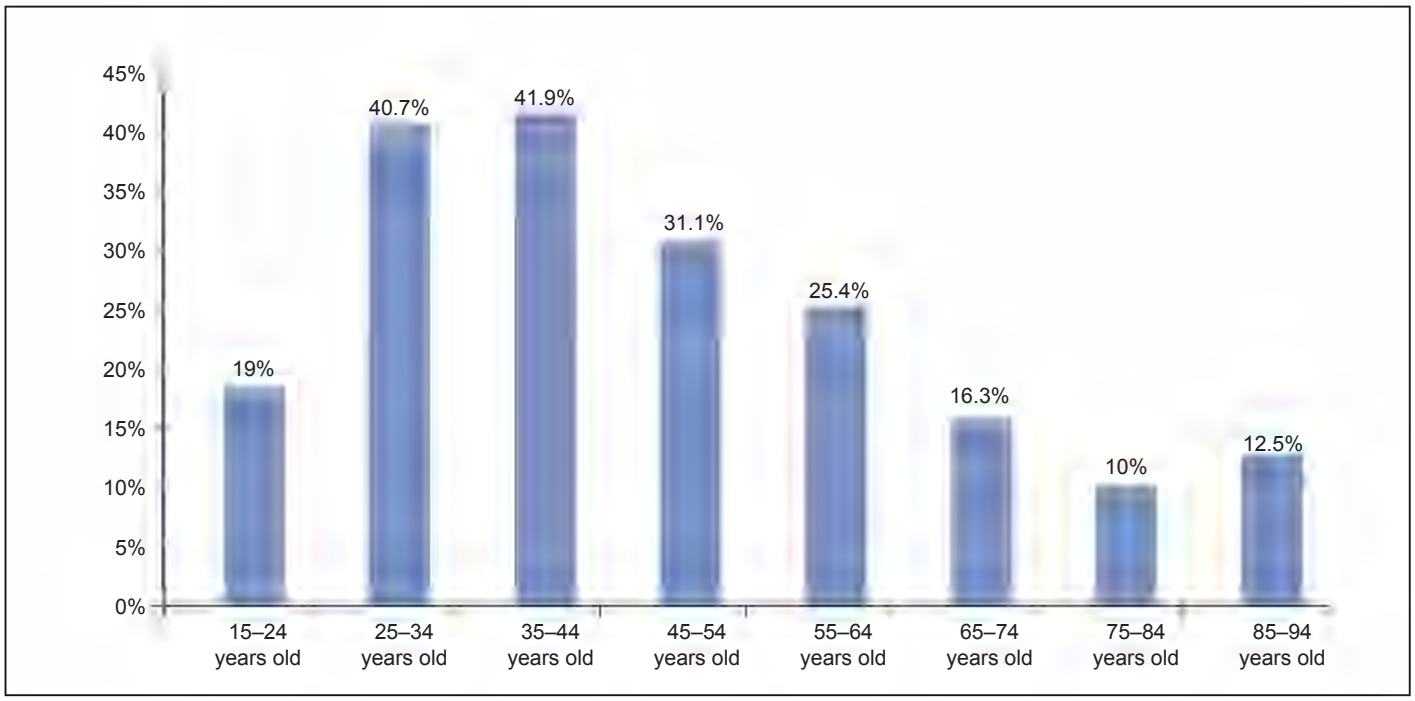
According to the guidelines of the Brazilian Health Ministry, the screening of lesions in the cervix should start at 25 years of age and end at 64[13,14]. In this study, when patients aged from 15 to 24 years were analyzed, 19% were found to have high-grade lesions. However, when patients aged 65 to 94 years were evaluated, 14.3% were found to have the said lesion, with this number being even more evident when only 65- to 74-year-olds were evaluated (16.3%). Consequently, according to this study, the target population determined by the Brazilian Ministry of Health would leave 16.2% women with high-grade lesions on the edge of a diagnosis, which corresponds to 11.3% of all high-grade cervical lesions, aged from 15 to 94 years. It is also known that a mere 30% Brazilian women undergo the screening of cervical cancer[15], which means it is likely that that there are an even higher number of women with high-grade lesions, in all age groups.

HPV infection has been more frequently reported among young, sexually active adults, between the ages of 18 and 25 years. When evaluating the natural history of the disease, we noticed that from the viral infection up to the appearance of an invasive carcinoma,

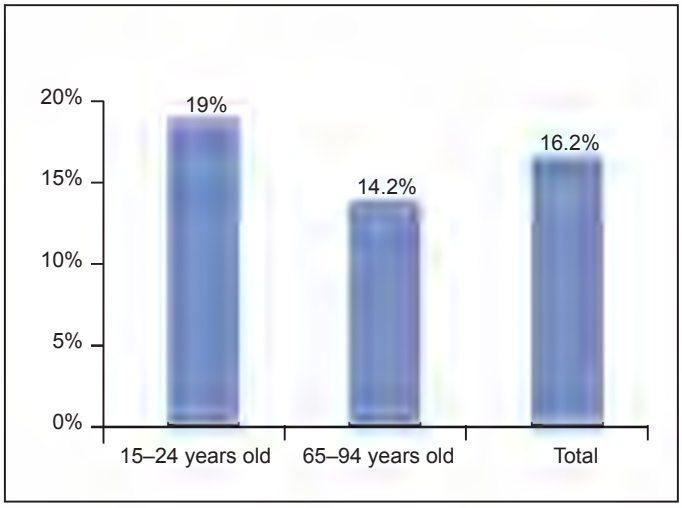
Table 1 – Number of patients per age group.

	15–24 years old	25–34 years old	35–44 years old	45–54 years old	55–64 years old	65–74 years old	75–84 years old	85–94 years old
Total	100	253	260	209	122	92	40	8
CIN 2 and 3	19	103	109	65	31	15	4	1
Percentage	19%	40.7%	41.9%	31.1%	25.4%	16.3%	10%	12.5%

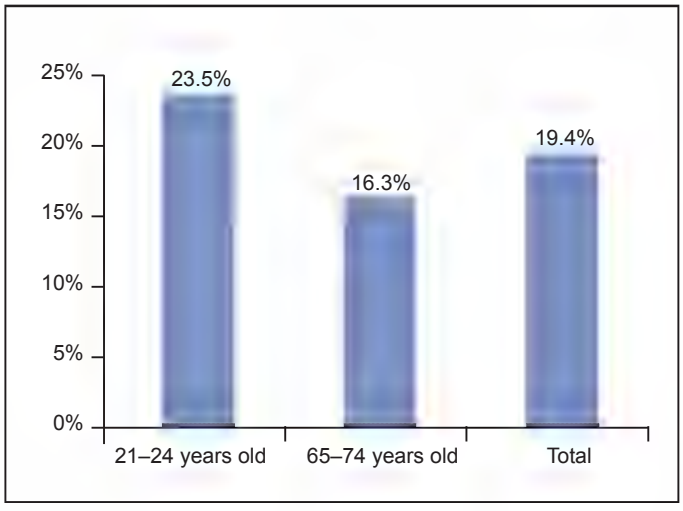
CIN: Cervical intraepithelial neoplasia.



Graph 1 – Prevalence of cervical intraepithelial neoplasia grade 2 and 3 for each age group.

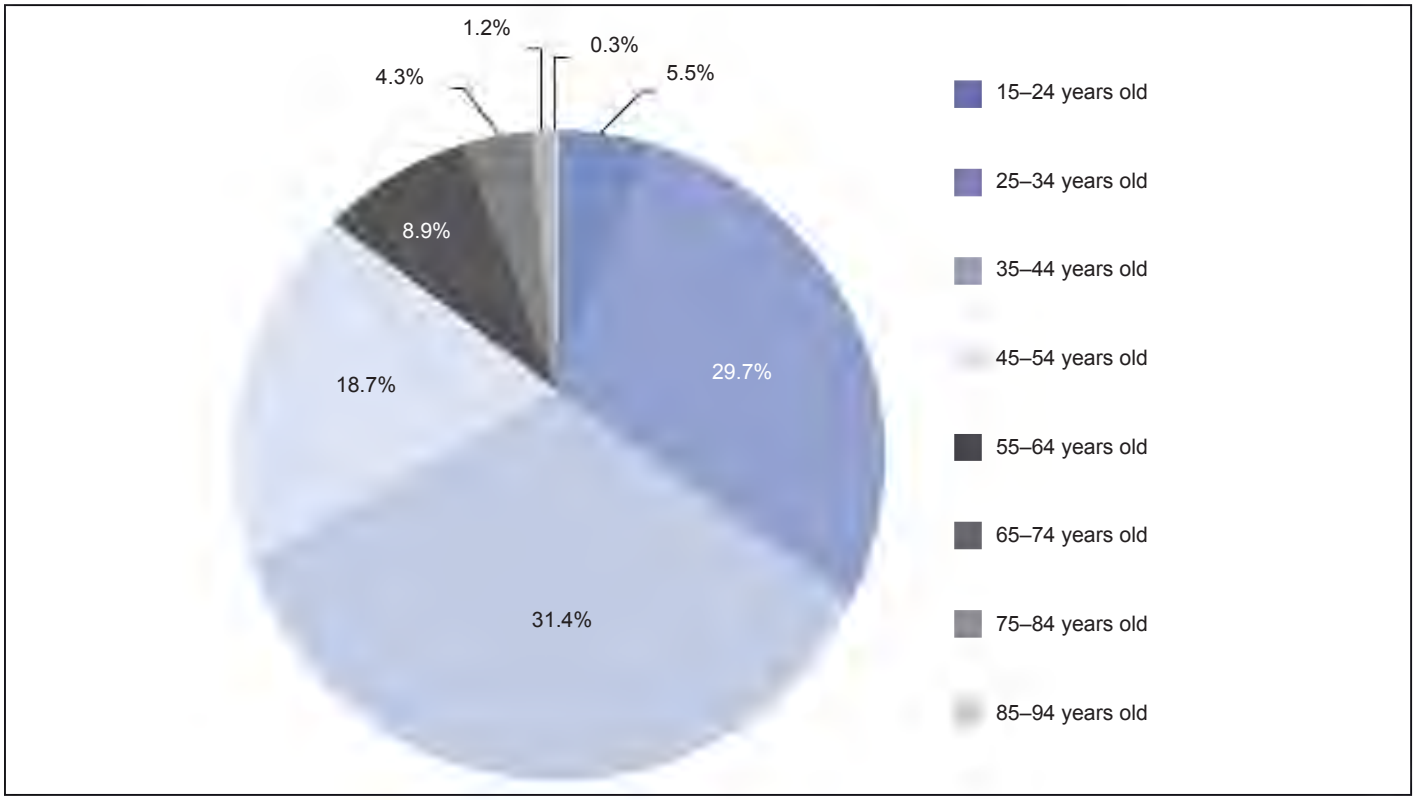


Graph 2 – Prevalence of cervical intraepithelial neoplasia grade 2 and 3 in those aged between 15–24 years and 65–94 years.

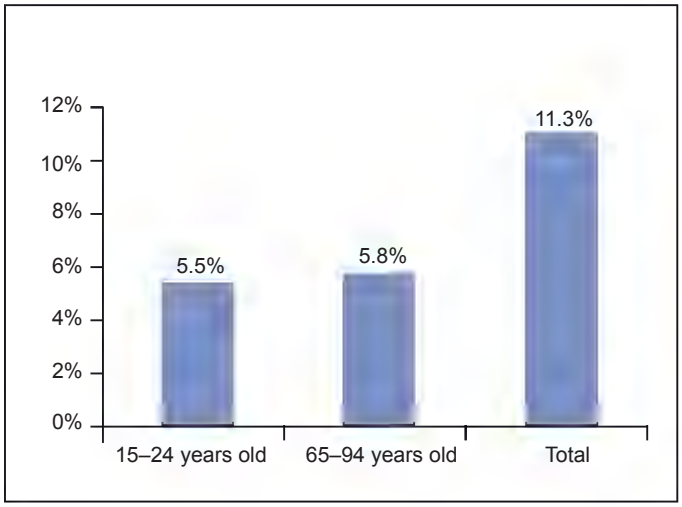


Graph 3 – Prevalence of cervical intraepithelial neoplasia grade 2 and 3 in those aged between 21–24 years and 65–74 years.

approximately 10 years passed. When the changes in the sexual behavior of the population are taken into consideration, mainly after the popularization of the medication against male impotence and female hormone therapy, and the decrease in the immunity or reactivation of the latent infection, mainly in elderly and immunosuppressed women[16], it is extremely important that we reflect on the existence of a new peak of incidence of later infection (therefore, a later appearance of these lesions) and discuss the necessity of amplifying the age group the screening covers, which has become more necessary in more advanced ages[12]. In this study, a significant number of patients over the age of 55 can be noted, revealing that a possible tendency in this direction will be exacerbated in the upcoming years. It is worth highlighting that the occurrence of CIN 2 and 3 in a 65-year-old patient, who would have been infected when around 55 years of age (allowing the possibility that she, currently, has an active sex life and new partners), is perfectly plausible and in line with the current reality. At this point, it is worth remembering that there is a tendency in amplifying the age group for women at a more advanced age due to a lack of studies, shown by the current recommendations from the WHO[13].



Graph 4 – Patients with cervical intraepithelial neoplasia grade 2 and 3 per age group.



Graph 5 – Percentage of patients with cervical intraepithelial neoplasia grade 2 and 3 from 15–24 years old and 65–94 years old, among the patients with this diagnosis.

In the case of the population under 25, with an initial sex life around 15 years of age, by 23 they could already have a premalignant or even a malignant lesion. A fact that is emphasized in the Brazilian population, which has estimates that indicate that more than 30% Brazilian women and around 47% Brazilian men initiate their sex life before the age of 14[17]. This premature start to a sex life leads some societies to opt for finding cytopathologic methods of the high-grade intraepithelial cervical lesions at 21 years of age, as was recommended in 2012 by the American Cancer Society, the American Society for Colposcopy and Cervical Pathology, and the American Society for Clinical Pathology[4].

Thus, returning to the results of our study, 23.5% patients between the ages of 21 to 24 have a high-grade cervical lesion. In the 15 to 25 age group, according to this study, 9.4% were found to have a high-grade lesion. These women would not be a part of the screening conducted by the Brazilian Ministry of Health. According to the folder, the reason for initiating the screening only at 25 years of age is based on studies that show even when cytology screening is performed in the young adult age group (21 to 24 years), there seems to be little to no impact in decreasing the number of cases of cervical cancer in screened or unscreened patients[18,19].

Regarding this age group of teenagers and young adults, some data are worth highlighting due to the importance of the infection in these groups. It is estimated that 13 to 38 % of young adults (20 to 24 years old), compared to 5 to 7% of those over 40 and sexually active, are infected by one or more types of HPV. This can be explained by the fact that this age group is initiating their sex life, a time at which there is characteristically a higher frequency of sexual activity, multiple partners, irregular use of barrier method contraceptives, and cervical fragility. Moreover, it is a known fact that having the first sexual encounter before the age of 18 is a risk factor for the development of cancer at an older age, with a risk three to four times higher of developing an invasive cancer compared to a first sexual encounter at 20 or older[20].

A detail from this younger age group is that younger women and teenagers still have not, in general, had offspring, and there is a discussion surrounding the increase in the risk of obstetric complications related to prior traditional conization, such as isthmus–cervical incompetence, leading to late abortion, premature labor, and/or low birth weight, when it cannot be avoided through cerclage[21-23].

It is noted, finally, that if in this population the patients from 21 to 24 and 65 to 74 years old were excluded, a total of 19.4% patients with high-degree lesions from these age groups and 8.9% among all high-grade lesions found would not have been a part of this diagnosis.

Regarding cervical cancer, it is relevant to know the prevalence of the disease and its behavior in each age group, and each population group, so that a deeper understanding of the profile of the disease can be had. This way, it becomes easier to equip the health-care system to decrease the frequency of the disease and produce progressively lower rates of invasive cervical cancer. The persistence of this neoplasia as an important cause of female mortality is unacceptable because it has a known natural history and, with the early diagnosis of the lesions, can be avoided in the majority of cases. Ample and early diagnoses of CIN 2 and 3 should, then, be prioritized, without forgetting that the public health groups should always be updated so as to mold their target population according to the changes in the population's needs and behavior[24].

Conflict of interests

The authors report no conflict of interests.

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