

# Iron deficiency is not the main contributor to anemia in older Mexican adults: results from the National Health and Nutrition Survey 2018-19

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## Abstract

**Objective.** To describe the current status of anemia and iron deficiency (ID), as well as associated sociodemographic characteristics, in older adults (OA). **Materials and methods.** Serum and capillary blood samples from a sample of OA participants (n=2 902) from the Ensanut 2018-19 were analyzed. ID was defined as s-ferritin <15 µg/L, and anemia was defined according to World Health Organization standards. Logistic regression models were used to associate the characteristics of OA with anemia and ID. **Results.** Of the OA analyzed, anemia was present in 28.4%, ID in 5% and iron deficiency anemia in 2.07%. Diabetes (OR=2.14), renal insufficiency (OR=10.4), higher age, and urban dwelling (OR=1.35) were conditions associated with higher odds for anemia (p<0.05). Belonging to the 70-79 year age group was the only condition associated with higher odds for ID (OR=1.86, p<0.05). **Conclusions.** Anemia affects a high proportion of OA, and ID is not the main contributor to anemia. Chronic comorbidities help explain the anemia problem in OA.

Keywords: iron; anemia; older adults; nutrition surveys; Ensanut 2018-19

De la Cruz-Góngora V, Rivera-Pasquel M, Shamah-Levy T, Villalpando-Hernández S. La deficiencia de hierro no es el principal contribuyente a la anemia en adultos mayores participantes en la Ensanut 2018-19. *Salud Publica Mex.* 2021;63:412-421. <https://doi.org/10.21149/12154>

## Resumen

**Objetivo.** Describir la situación actual de deficiencia de hierro (DH), anemia y características asociadas en adultos mayores (AM). **Material y métodos.** Se analizó información de 2 902 AM de la Ensanut 2018-19. Deficiencia de hierro se definió: s-ferritina <15 µg/L y anemia de acuerdo con el criterio de la Organización Mundial de la Salud. Se emplearon modelos de regresión logística para identificar las características asociadas con la DH y anemia en los AM. **Resultados.** La prevalencia de anemia fue de 28.4%, DH 5% y anemia por DH 2.07%. Diabetes (RM=2.14), insuficiencia renal (RM=10.4), la mayor edad y habitar en localidades urbanas (RM=1.35) se asociaron a mayor momio para anemia (p<0.05). El grupo de edad de 70-79 años fue la única característica asociada a mayor probabilidad de DH (RM=1.86, p<0.05). **Conclusiones.** La anemia afecta a una proporción de los AM sin tener como principal causa a la DH. Algunas comorbilidades crónicas explican el problema de la anemia en esta población.

Palabras clave: hierro; anemia; adultos mayores; encuestas nutricionales; Ensanut 2018-19

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Around the world, the number, and the proportion of older adults (OA, defined as those aged 60 or more years) is increasing. Approximately 400 million OA are estimated to live in low-income countries; by 2025, this number is expected to reach more than 1.2 billion.<sup>1</sup> In Mexico, according to the National Dynamic Demographic Survey 2018, there are 15.4 million OA, who amount to 12.3% of the total population.<sup>2</sup> OA undergo physiological, and social changes associated with aging that make them vulnerable to malnutrition: particularly to micronutrient deficiencies.<sup>3</sup>

Iron deficiency (ID) is the most commonly occurring and prevalent nutritional disorder worldwide, and OA are among the affected.<sup>3</sup> ID in OA may stem from inadequate dietary intake of iron, poor absorption, excessive losses, or a combination of these factors, and it is a principal cause of nutritional anemia.<sup>4</sup> In OA, ID without anemia has been associated with health consequences negatively affecting survival, particularly among those with a cardiovascular disease.<sup>5,6</sup> On the other hand, anemia in OA has been associated with cognitive impairment,<sup>7</sup> frailty, a decline in physical performance,<sup>8</sup> and an increased susceptibility to falls,<sup>9</sup> among other consequences which affect quality of life<sup>9</sup> and survival.<sup>10</sup> According to the Mexican National Health and Nutritional Survey 2012 (Ensanut 2012), the prevalence of anemia in OA in Mexico was 16.5%, affecting 1 out of every 3 OA of 80 years or more (30%) and 1 out of every 5 OA in the southern region of Mexico.<sup>11</sup> In the elderly, anemia has many causes, the most frequent being associated with chronic diseases (ACD). ACD is characterized by low grade chronic inflammation, which affects iron availability for erythropoiesis in bone marrow.<sup>12</sup>

In Mexico, overweight and obesity have risen in the last several decades, affecting around 74% of OA; self-reported diabetes and arterial hypertension (HTN) affect 25 and 42.2% of OA,<sup>13</sup> respectively, while 7% of OA are affected by arthritis,<sup>14</sup> 16.3 by renal disease, and 55.6% by multimorbidities.<sup>15</sup> This profile of chronic comorbidities in older Mexican adults, alongside aging processes, promotes a pro-inflammatory response that may increase the risk of ACD.<sup>16</sup>

Anemia in the elderly has become a public health issue and monitoring its trends and identifying its main risk factors have become necessary to direct public health response. Therefore, the main objective of this study is to describe and update the prevalence of ID and anemia in a subsample of OA who participated in the Mexican National Health and Nutritional Survey 2018-19 (Ensanut 2018-19), as well as characterize other

associated sociodemographic factors. In addition, this study aims to highlight the changes between these two indicators from the application of the Ensanut 2012 to that of the 2018-19.

## Materials and methods

### Design and study population

This is a cross-sectional study based on information from 2 902 participants representing 15 593 500 OA ( $\geq 60$  years of age), all whom were participants in the Ensanut 2018-19 in which complete serum data were analyzed. This subsample of OA is representative at the national level and is disaggregated by area and geographic region. All data was collected through standardized procedures using *ad hoc* questionnaires and trained staff. Further details on sample selection and procedures related to the Ensanut 2012 and Ensanut 2018-19 surveys are described in Romero M and colleagues.<sup>13</sup>

### Sociodemographic information

Sociodemographic information was collected using *ad hoc* questionnaires. Mexico was divided into three geographic regions: North, Central and Mexico City, and South. Indigenous ethnicity was defined as the head of the household self-reporting knowledge of an indigenous language. Dwelling type was classified as urban for localities with  $\geq 2$  500 inhabitants, and rural for those with  $\leq 2$  500 inhabitants. A household wealth index (HWI) was generated using a principal components analysis that included variables such as housing conditions, flooring and roofing materials, ownership of home appliances and electronics, and number of rooms. The first component of the analysis explained 51% of the variability with a lambda of 4.078. The resulting standardized index was divided into tertiles, the first of which represents the poorest conditions. Information regarding eligibility and use of a social assistance program (Liconsas) was obtained through a questionnaire.

### Anthropometry

Weight and height data were collected using validated and standardized methods.<sup>17,18</sup> The body mass index (BMI) was calculated as total weight in kilograms divided by the square of height in meters. BMI classification was based on World Health Organization (WHO) cutoff points for adults.<sup>19</sup>

## Self-reported health conditions

Diabetes and renal insufficiency (RI) were registered if previously diagnosed by a physician.

## Supplement consumption

Data on consumption of any type of micronutrient supplements was obtained through a Food Frequency Questionnaire (FFQ) with the period of reference of seven days prior to the survey.

## Biochemical determinations

Venous blood samples were drawn from the antecubital vein and collected in vacuum tubes in 30% of the total OA participants. Serum was separated and spun *in situ* at 3 000 g in a portable centrifuge. Cryovials were immediately frozen using liquid nitrogen (-20°C) in Dewar flasks until delivery to the Biochemistry Nutrition Laboratory of the National Institute of Public Health of Mexico (INSP, in Spanish), in Cuernavaca, Morelos, where they were stored in freezers at -70°C. Serum ferritin concentrations were measured by chemiluminescent microparticle immunoassay, and the C-reactive protein (CRP) was measured by immunoassay with ultrasensitive monoclonal antibodies using Abbott commercial kits (Abbott Architect). Measurements were performed with an automatic analyzer (Architect i2000, Abbott Diagnostic, Wiesbaden, Germany). The intra-assay variability for ferritin was 3.35, and for CRP, 4.4%. Serum ferritin concentrations were adjusted for inflammation (multiplying factor: 0.65) when CRP levels were >5 mg/L, as described by Thurnham.<sup>20</sup>

Hemoglobin (Hb) concentrations were measured with capillary blood collected by finger prick using a portable photometer (Hemocue 201+, Alghen, Sweden).

Anemia was defined as Hb concentration adjusted by altitude<sup>21</sup> of <12 g/dL for women or <13 g/dL for men.<sup>22</sup>

ID was defined as serum ferritin adjusted by CRP of <15 µg/dL.<sup>23</sup> Iron deficiency anemia (IDA) was defined as the coexistence of anemia and ID.<sup>23</sup>

## Statistical analysis

All analyses are presented as frequencies with 95% confidence intervals (CI). Bivariate analysis by the conditions of anemia and ID were performed by logit regression.

To identify the sociodemographic characteristics associated with ID, logistic regression models were adjusted by sex, age group, BMI, dwelling type, indigenous ethnicity, geographic region, tertile of HWI, diabetes, renal insufficiency (RI), CRP>5 mg/L and ID in the ane-

mia model. All analyses considered the complex survey design and were completed using Stata v15. Statistical significance was set at alpha=0.05.

## Ethics

This study was conducted according to the guidelines set by the Declaration of Helsinki. The survey protocol was approved by the committees of Research, Ethics and Biosecurity of the INSP. Written informed consent was obtained from all OA survey participants.

## Results

Table I shows the characteristics of older Mexican adults with serum information. Fifty-four percent of OA were in the 60-69-years age group and were female, 7.6% spoke an indigenous language, 28.4% had CRP levels above 5 mg/L, 27% had diabetes, and 3% had renal insufficiency. In a subsample of OA, 24% were taking some form of nutritional supplement.

## Anemia

Anemia was present in 28.4% (CI95% 25.9-30.9) of OA. The bivariate analysis showed that anemia prevalence was significantly higher in those of relatively higher age (90+ years), as well as in those with CRP>5 mg/L or with a diagnosis of diabetes, renal insufficiency, or AD, and in those consuming supplements ( $p<0.05$ ), in comparison with their counterparts. On the contrary, lower anemia prevalence was observed in those with obesity and those within the third HWI tertile (table II).

Adjusted models in which the characteristics mentioned above remained associated to anemia showed similar results. Relatively older age ( $p<0.005$ ), urban dwelling (OR=1.35,  $p=0.038$ ), living in the southern region (OR=0.64,  $p=0.012$ ) and diagnosis of diabetes (OR=2.14,  $p<0.001$ ) or renal insufficiency (OR=10.4,  $p<0.001$ ) were all conditions associated with higher odds for anemia. A marginally significant association was observed in the presence of CRP levels >5 mg/L (OR=1.36,  $p=0.067$ ) and ID (1.67,  $p=0.07$ ). In contrast, higher HWI ( $p<0.05$ ) and obesity (OR=0.7,  $p=0.08$ , marginally significant), were characteristics associated to lower odds for anemia compared with their respective counterparts of HWI tertile and normal BMI (table III).

## Iron deficiency

The prevalence of ID in OA was 5.0% (CI95% 3.9, 6.3). In the bivariate analysis, relatively older age and anemia



**Table II**  
**PREVALENCE OF ANEMIA AND IRON DEFICIENCY IN OLDER MEXICAN ADULTS, BY SOCIODEMOGRAPHIC CHARACTERISTIC. MEXICO, ENSANUT 2018-19**

	Anemia			Iron deficiency		
	Expansion			Expansion		
	<i>N (thousands)</i>	%	<i>CI95%</i>	<i>N (thousands)</i>	%	<i>CI95%</i>
National	4 397.1	28.4	(25.9-30.9)	773.5	5	(3.9-6.3)
Age group (years)						
60-69	1 847.3	21.9	(18.9-25.2)	299.1	3.5	(2.4-5.1)
70-79	1 538.7	31.9	(27.3-36.8)	319.5	6.6	(4.6-9.4)
80-89	804.3	44.3	(36.2-52.6)	153.7	8.3	(4.4-15.1)
90+	206.7	50	(28.3-71.6)	1.2	0.3	(0.0-2.0)
Sex						
Male	1 950.4	27.6	(23.9-31.6)	311.8	4.4	(3.0-6.5)
Female	2 446.6	29	(25.6-32.6)	461.6	5.4	(4.0-7.4)
Dwelling type						
Rural	882.3	25.6	(22.6-28.9)	170.3	4.9	(3.5-7.0)
Urban	3 514.8	29.2	(26.2-32.3)	603.1	5	(3.7-6.7)
Geographic region						
Northern	1 008.4	31.7	(27.3-36.5)	161.2	5	(3.3-7.7)
Center and Mexico City	2 133.7	28.3	(24.4-32.5)	451.2	6	(4.3-8.3)
Southern	1 255.0	26.3	(22.5-30.5)	161	3.4	(1.9-5.9)
Tertile of household wealth index						
Tertile 1	1 650.6	32.5	(28.6-36.6)	283.4	5.5	(3.7-8.2)
Tertile 2	1 452.9	29.3	(24.8-34.2)	236.4	4.8	(3.2-7.1)
Tertile 3	1 293.6	23.7	(19.3-28.9)	253.7	4.6	(2.9-7.4)
Indigenous						
No	4 072.8	28.4	(25.8-31.2)	715.9	5	(3.8-6.4)
Yes	324.3	27.9	(21.4-35.4)	57.5	4.9	(2.5-9.5)
Body mass index						
Underweight	80.4	50.1	(30.4-69.8)	4.8	3	(0.7-11.6)
Normal	1 067.7	29	(24.4-34.1)	225.4	6.1	(3.6-10.0)
Overweight	1 681.8	28.3	(24.2-32.7)	281.7	4.7	(3.1-7.1)
Obese	1 015.2	21.4	(17.5-26.0)	207.2	4.4	(2.9-6.5)
Beneficiary of social assistance program <i>Liconsa</i>						
No	4 097.2	28.2	(25.7-30.9)	737.4	5.1	(3.9-6.5)
Yes	289.5	29.9	(18.4-44.6)	36.1	3.7	(1.4-9.6)
C-reactive protein >5 mg/L						
No	2 960.0	26.6	(23.8-29.6)	534.4	4.8	(3.5-6.5)
Yes	1 425.8	32.6	(27.8-37.9)	239	5.4	(3.6-8.0)
Diabetes						
No	2 733.0	24.3	(21.5-27.2)	556.8	4.9	(3.7-6.6)
Yes	1 635.6	39.1	(33.8-44.7)	209.7	5	(3.2-7.8)

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Renal insufficiency						
No	3 987.8	26.6	(24.3-29.1)	758.7	5	(3.9-6.5)
Yes	380.8	82	(69.3-90.2)	7.8	1.7	(0.4-6.7)
Supplement consumption						
No	901.1	30.5	(24.8-37.0)	100.4	3.4	(1.9-6.1)
Yes	419.2	44.3	(32.4-56.9)	95.3	10.1	(5.1-19.1)
Iron deficiency						
No	4 065.8	27.7	(25.2-30.3)	-	-	-
Yes	320.1	41.5	(30.0-53.9)	-	-	-
Anemia						
No	-	-	-	451.4	4.1	(2.9-5.7)
Yes	-	-	-	320.1	7.3	(5.1-10.3)

Ensanut: Encuesta Nacional de Salud y Nutrición

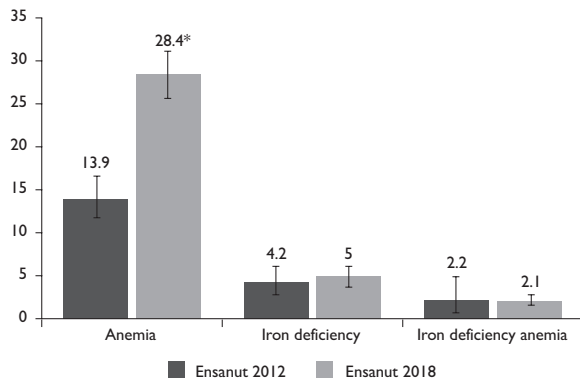
**Table III**  
**LOGISTIC REGRESSION MODEL OF SOCIODEMOGRAPHIC CHARACTERISTICS ASSOCIATED WITH ANEMIA AND IRON DEFICIENCY IN OLDER MEXICAN ADULTS. MEXICO, ENSANUT 2018-19**

n	Anemia		Iron deficiency	
	OR	CI95%	OR	CI95%
N (thousands)	14 452.19		14 259.03	
Age group in years (reference: 60-69)				
70-79	1.68	(1.2-2.3)	1.86	(1.0-3.3)
80-89	2.74	(1.8-4.3)	1.61	(0.6-4.1)
90+	2.06	(0.8-5.4)	na	
Sex (female=1)	1.03	(0.8-1.4)	1.25	(0.7-2.2)
Dwelling type (urban=1)	1.35	(1.0-1.8)	1.3	(0.7-2.5)
Tertile of HWI* (reference: tertile 1)				
Tertile 2	0.68	(0.5-1.0)	0.78	(0.4-1.6)
Tertile 3	0.51	(0.3-0.8)	0.64	(0.3-1.4)
Geographic region (reference: Northern)				
Center and Mexico City	0.75	(0.5-1.0)	1.09	(0.6-2.0)
Southern	0.64	(0.4-0.9)	0.6	(0.3-1.3)
C-reactive protein>5 mg/L (yes)	1.36	(1.0-1.9)	1.31	(0.7-2.3)
Iron deficiency (yes)	1.67	(1.0-2.9)	-	
Body mass index (reference: normal)				
Underweight	1.97	(0.7-5.2)	0.33	(0.1-1.7)
Overweight	1.06	(0.8-1.5)	0.79	(0.4-1.5)
Obese	0.7	(0.5-1.1)	0.69	(0.3-1.4)
Diabetes (yes)	2.14	(1.6-2.9)	0.98	(0.5-1.7)
Renal insufficiency (yes)	10.39	(4.8-22.3)	0.44	(0.1-1.9)
Intercept	0.27	(0.2-0.4)	0.05	(0-0.1)

\* Household Wealth Index

Ensanut: Encuesta Nacional de Salud y Nutrición





\* Statistically significant

ENSANUT: Encuesta Nacional de Salud y Nutrición

**FIGURE 1. COMPARISON OF THE PREVALENCE OF ANEMIA, IRON DEFICIENCY AND IRON DEFICIENCY ANEMIA IN OLDER MEXICAN ADULTS IN THE SUBSAMPLE WITH SERUM DATA. MEXICO, ENSANUT 2012 AND 2018**

Iron status has been the only micronutrient indicator studied in all age groups within the Mexican population, because ID is considered to be a main contributor to anemia worldwide, including in OA. Prevalence of ID in this study was very similar to that reported in OA of the Mayan region (5%)<sup>28</sup> and lower to that reported in the Portuguese OA population (~15%),<sup>29</sup> using the same cutoffs for ferritin. In a nationally representative sample of OA aged >50 years using higher cutoff values for ferritin levels (<30 µg/L), ID prevalence was reported in 8.8% of the population analyzed.<sup>30</sup> In addition, the low proportion of IDA in the present study is similar to other reports which use the same cutoff values.<sup>31</sup> ID, independent of the condition of anemia, has negative consequences on health which in OA are mainly linked to weakness, depression, cardiovascular disease, hospitalization, impaired cognition, and mortality, among other outcomes.<sup>5,30,32-34</sup> If the deficiency is not treated, progressive health consequences may become irreversible. Identifying absolute ID in OA population presents a challenge because metabolic iron indicators, like ferritin, may lead to misdiagnosis in this population.<sup>35</sup> In inflammatory conditions, iron sequestration occurs due to the presence of hepcidin, a protein synthesized by the liver during infections provoked by a continuous stimulus of IL-6, which blocks iron export from cells and leads to sequestration of iron into ferritin.<sup>36</sup> Ferritin levels subsequently increase; however, they do not promote sufficient iron incorporation into erythroid precursors even in the presence of adequate bodily iron stores, and therefore they lead to functional ID.<sup>27</sup> Some statistical approaches attempt to correct ferritin values by a) ad-

justing for inflammation biomarkers such as CRP and alpha glycoprotein 1 acid, b) excluding subjects with some degree of inflammation, or c) increasing the cutoff value of serum ferritin to 70 mcg/L.<sup>37</sup> Others consider alternative iron indicators, such as serum transferrin receptor.<sup>38</sup> Nonetheless, no consensus has been reached to allow a standardized diagnosis of ID in OA. According to WHO cutoff thresholds, ID prevalence in older Mexican adults is low and may be underestimated when compared to the magnitude of anemia reported in this population. Both the ID cutoff values proposed by the WHO and the adjustment factors used for ferritin were derived from studies performed with women and children.<sup>20,37</sup> Therefore, population based studies are needed to properly identify the best iron indicators for epidemiological studies seeking to define ID in the aging population.

In this study, higher CRP values, indicative of some degree of inflammation, were associated to anemia, which reinforces our initial approach regarding AI. Nevertheless, we did not have sufficient information regarding other inflammatory biomarkers or other health indicators to allow proper definition of AI. Diabetes was a prevalent condition affecting a third of OA, and was associated to anemia but not to ID, which may indicate that diabetic kidney disease may play a role in such an association.<sup>39</sup> Renal insufficiency results in the failure of the kidneys to produce erythropoietin, affecting erythropoiesis and deriving in anemia. This explains the marked association of RI to anemia, even when RI was present only in a low proportion of OA. In OA with diabetes and RI, anemia and glycemic control should be screened to avoid the negative health consequences associated.<sup>40</sup>

Other potential contributors known to be associated with anemia and ID were not analyzed in the present study; these include, among others, drug consumption, vitamin B12 deficiency, inherited Hb disorders, and gastrointestinal bleeding, which may have revealed potential factors explaining the high rate of anemia in this elderly population. In the Mayan region, anemia among the elderly was partially explained by inflammatory conditions, followed by chronic renal disease, although a high proportion of anemias did not have a clear cause.<sup>28</sup> In the same study, diabetes was strongly associated with AI, while nutritional causes exhibited the lowest contribution.

The present study explores for the first time certain chronic comorbidities, such as renal insufficiency previously diagnosed by a physician, as potential contributors to explain the condition of anemia in OA. Even when diabetes and RI could be potential causes of anemia, such conditions do not explain the high rate

of anemia observed in this population, a fact that highlights the importance of interpreting changes between different surveys with caution.

The results presented have some limitations. First, due to the cross-sectional design, temporality is limited, and reverse causality may explain the variables associated to anemia. The anemia in this elderly population may be the result of diverse chronic comorbidities not fully explored in the present study. Second, some measurement error in Hb estimation may explain the prevalence of anemia observed.<sup>41</sup> The 201+ model of Hemocue used in the present survey has not been validated in our population; nevertheless, some studies have reported that this model achieves better performance in comparison with other Hemocue models.<sup>42,43</sup> Therefore, caution is advised in the interpretation of the results presented.

Anemia and ID are reversible conditions at the population level. In OA, anemia is a predictor for worse prognosis in the short term compared to ID<sup>44</sup> and is associated to increased healthcare costs;<sup>45</sup> therefore, the burden of anemia in OA may saturate healthcare services if no actions are taken. The present results may have implications in research and in public health: first, clinical research would provide insights on the potential causes of anemia in OA that are difficult to measure at the population level.<sup>46</sup> Second, food policies are necessary to address the achievement of optimal nutrition in OA in order to prevent not only micronutrient deficiencies but also chronic comorbidities that affect healthy aging. Finally, intervention studies with integrative approaches are needed to promote healthy aging in the Mexican population.<sup>47</sup> Several research gaps still remain which prevent from properly addressing the problem of anemia and micronutrient deficiencies in Mexico. In OA, the causes of anemia are still not fully known; in addition, the cutoff values used to define anemia, ID and ferritin value adjustment factors for inflammation were not originally designed for the elderly population.<sup>48,49</sup> Therefore, longitudinal studies are needed to define for this age group the optimal cutoff values for anemia and ID that will improve the prognosis of certain outcomes associated with healthy aging.

## Conclusions

In conclusion, results from the subsample of OA participants in this study show that anemia affects a high proportion of OA, and that ID is not the main contributor to this prevalence of anemia. Chronic comorbidities such as diabetes and renal insufficiency contribute to the anemia issue. Further studies are needed to understand

the potentially modifiable causes of anemia in older Mexican adults.

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*Declaration of conflict of interests.* The authors declare that they have no conflict of interests.

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