



# Transcranial Doppler ultrasonography to evaluate cerebral hemodynamic changes in neurocysticercosis

## *Ultrasonografía Doppler transcraneal para evaluar cambios hemodinámicos cerebrales en neurocisticercosis*

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Arq. Neuro-Psiquiatr. 2024;82(7):s00441788584.

### Abstract

**Background** Arteritis is a complication of neurocysticercosis (NCC), which is not well known and could trigger strokes. The transcranial Doppler ultrasound (TCD) is a noninvasive method for detecting, staging, and monitoring cerebrovascular diseases. Nonetheless, the utility of TCD to evaluate cerebral hemodynamic changes, suggesting vasculitis associated with NCC remains uncertain.

**Objective** To evaluate cerebral hemodynamic changes using TCD in patients with subarachnoid and parenchymal NCC.

**Methods** There were 53 patients with NCC evaluated at a reference hospital for neurological diseases included (29 with subarachnoid and 24 with parenchymal). Participants underwent a clinical interview and serology for cysticercosis and underwent TCD performed within 2 weeks of enrollment. Mean flow velocity, peak systolic velocity, end diastolic velocity, and pulsatility index were recorded.

**Results** Among the participants, there were 23 (43.4%) women, with a median age of 37 years (IQR: 29–48). Cerebral hemodynamic changes suggesting vasculitis were detected in 12 patients (22.64%); the most compromised vessel was the middle cerebral artery in 11 (91.67%) patients. There were more females in the group with sonographic signs of vasculitis (10/12, 83.33% vs. 13/41, 31.71%;  $p = 0.002$ ), and this

### Keywords

- ▶ Neurocysticercosis
- ▶ Cysticercosis
- ▶ Ultrasonography, Doppler, Transcranial
- ▶ Stroke
- ▶ Vasculitis

received  
November 11, 2023  
received in its final form  
April 04, 2024  
accepted  
April 27, 2024

DOI <https://doi.org/10.1055/s-0044-1788584>.  
ISSN 0004-282X.

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Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

was more frequent in the subarachnoid NCC group (9/29, 31.03% vs. 3/24, 12.5%;  $p = 0.187$ ), although this difference did not reach statistical significance.

**Conclusion** Cerebral hemodynamic changes suggestive of vasculitis are frequent in patients with NCC and can be evaluated using TCD.

## Resumen

**Antecedentes** La arteritis es una complicación de la neurocisticercosis (NCC), que no siempre se conoce y podría desencadenar enfermedad cerebrovascular. La ultrasonografía Doppler transcraneal (DTC) es un método no invasivo que sirve para detectar y monitorizar enfermedades cerebrovasculares. No obstante, la utilidad de la DTC para evaluar los cambios hemodinámicos cerebrales que sugieren vasculitis asociada a NCC sigue siendo incierta.

**Objetivo** Evaluar los cambios hemodinámicos cerebrales utilizando DTC en pacientes con NCC subaracnoidea y parenquimal.

**Métodos** Se incluyeron 53 pacientes con NCC (29 con subaracnoidea y 24 con parenquimal) evaluados en un hospital de referencia para enfermedades neurológicas. Los participantes se sometieron a una entrevista clínica y serología para cisticercosis y a una DTC realizada dentro de las 2 semanas posteriores a la inscripción. Se registraron la velocidad media del flujo, la velocidad sistólica máxima, la velocidad diastólica final y el índice de pulsatilidad.

**Resultados** Los participantes incluyeron 23 (43,4%) mujeres con una mediana de edad de 37 años (rango intercuartílico [RIC]: 29–48). Se detectaron cambios hemodinámicos cerebrales sugestivos de vasculitis en 12 pacientes (22,64%); el vaso más comprometido fue la arteria cerebral media, en 11 (91,67%) pacientes. Hubo más mujeres en el grupo con signos ecográficos de vasculitis (10/12, 83,33% *versus* 13/41, 31,71%;  $p = 0,002$ ), y esto fue más frecuente en el grupo de NCC subaracnoidea (9/29, 31,03% *versus* 3/24, 12,5%;  $p = 0,187$ ), aunque esta diferencia no alcanzó significancia estadística.

**Conclusión** Los cambios hemodinámicos cerebrales sugestivos de vasculitis son frecuentes en pacientes con NCC y pueden evaluarse mediante DTC.

## Palabras clave

- ▶ Neurocisticercosis
- ▶ Cisticercosis
- ▶ Ultrasonografía Doppler Transcraneal
- ▶ Enfermedad Cerebrovascular
- ▶ Vasculitis

## INTRODUCTION

Neurocysticercosis (NCC) is the most common parasitic infection of the central nervous system (CNS) and is present mainly in developing countries, being the cause of around 30% of secondary epilepsies.<sup>1,2</sup> In Latin America, approximately 75 million people live in NCC-endemic regions, 400 thousand of whom are affected by the symptomatic disease.<sup>3</sup>

This infection occurs in parenchymal and extraparenchymal forms, with the latter involving the ventricular and subarachnoid spaces. The clinical presentation of NCC varies depending on the parasitic burden, location, size, degree of degeneration, and immune response of the host. Seizures, chronic headaches and intracranial hypertension are the most frequent manifestations.<sup>2</sup> Cerebral cysticercotic vasculitis (CCV) is a less recognized complication of this infection and is predominantly documented in the subarachnoid form,<sup>4,5</sup> having been documented through the use of angiography in 53% (15/28) of patients with subarachnoid NCC.<sup>6</sup> Furthermore, CCV can result in strokes and, in some cases, brain hemorrhage.<sup>7</sup> The frequency of cerebral infarctions associated with NCC varies from 2 to 15%.<sup>8,9</sup> The mechanisms

discussed that have implications on the cerebrovascular disease are an occlusive endarteritis secondary to basal exudates on the subarachnoid space, thrombosis of the superficial cortical vessels due to chronic meningitis, and segmental vasculitis of blood vessels due to an adjacent cyst.<sup>4,5,8,10,11</sup>

The transcranial Doppler (TCD) ultrasound is a noninvasive method for evaluating the blood flow velocity of the main intracranial arteries allowing the indirect detection of vasculitis. It is inexpensive and reproducible, even in critically ill patients, making this tool an important test for the detection, staging, and monitoring of cerebrovascular disease. The TCD has been shown to be valuable in different cerebrovascular pathologies, such as intracranial artery stenosis, monitoring of vasospasm, and cerebral circulatory arrest. Furthermore, this ultrasound has a sensitivity and specificity of 95% for detecting intracranial stenosis of major vessels in patients with ischemic stroke, with variations depending on the temporal bone thickness.<sup>12,13</sup> In relation to its use in NCC, the information is currently scarce, and the only published prospective study included 9 individuals with

subarachnoid NCC and cerebral infarction, and arteritis was detected by TCD in 7 of 10 arterial lesions that were also detected by digital subtraction angiography, suggesting that TCD is a promising tool for the diagnosis and follow-up of CCV.<sup>4</sup>

Although TCD is a useful tool in the diagnosis and follow-up of intracranial vasculitis of various etiologies,<sup>13,14</sup> information is still scarce regarding the use of TCD to detect CCV in patients with subarachnoid and parenchymal NCC. This study aimed to evaluate cerebral hemodynamic changes suggesting vasculitis in patients with subarachnoid and parenchymal neurocysticercosis by using TCD.

## METHODS

We conducted a cross-sectional study approved by the Institutional Review Board of Instituto Nacional de Ciencias Neurológicas (INCN), a reference center for neurological diseases in Lima, Peru. A total of 53 consecutive NCC patients were included, 29 with subarachnoid and 24 with parenchymal, who were evaluated at the INCN outpatient clinic before starting antiparasitic treatment. Included subjects had NCC lesions evidenced in magnetic resonance imaging (MRI), confirmed by specific serology using enzyme-linked immunoelectrotransfer blot (EITB), fulfilling the diagnostic criteria.<sup>15</sup> The exclusion criteria were history of cerebrovascular disease or intracranial vasculitis attributable to other causes, and focal deficit. The presence of arachnoiditis was assessed using postcontrast MRI.

The sonographic diagnosis of CCV was defined by the identification of stenosis or occlusion along a blood vessel using TCD with a 2-MHz transducer from DWL (Multidopp T. 0801, 2006). The procedure was performed by one vascular neurologist trained in ultrasonography, blinded to the clinical and neuroimaging findings of the participants. The arteries were evaluated in two windows: the middle cerebral artery (MCA), anterior cerebral artery (ACA), and posterior cerebral artery (PCA) were evaluated through the temporal window, while the basilar artery was evaluated through the suboccipital window. Alterations in the mean velocities consistent with stenosis or occlusion have been described in previous studies.<sup>13,16</sup>

Each artery was evaluated along the blood vessels. For the MCA, 6 segments were considered from 65 to 40 mm in depth; for the ACA, 3 segments, from 65 to 75 mm in depth; the PCA was evaluated in 3 segments, from 55 to 65 mm in depth; and the basilar artery, in 6 segments, from 75 to 100 mm in depth. The diagnostic criteria for stenosis of the middle and anterior cerebral arteries were the peak systolic velocity (PSV) greater than 140 cm/s and the mean velocity (MV) greater than 80 cm/s in at least one segment. The criteria for basilar artery and PCA stenosis were mean blood flow velocities greater than 65 cm/s and 70 cm/s respectively.<sup>16,17</sup>

Patient characteristics were described as summary statistics, with categorical variables being expressed as percentages, whereas continuous and discrete variables were expressed using mean  $\pm$  standard deviation (SD) or median and ranges, respectively. Normality assessment was per-

formed using the Shapiro-Wilk test and comparisons between groups was performed by the Student *t*-test in cases of quantitative variables with normal distribution or by the Mann-Whitney U test. Additionally, the Chi-squared, and Fisher exact tests were used for categorical variables. Statistical significance of the test was set at 0.05. The analysis was performed using Stata (StataCorp LLC., College Station, TX, USA), version 17.0.

## RESULTS

The participants had a median age of 37 years (interquartile range [IQR]: 29–48) and 23 (43.40%) were females. Of the 53 total, 29 patients had subarachnoid NCC and 23 had parenchymal NCC. The median duration of illness before enrollment was 36 months (IQR: 12–120). Headache was the most common manifestation, presenting as the first symptom in 25 of the patients (48.04%). None had focal deficit. 11 (25.58%) patients had used steroids in the last 6 months, and 4 (9.09%) patients were using steroids at enrollment. The median body mass index (BMI) was 24.82 (IQR: 22.89–26.77). The median number of reactive antibody bands on EITB was 7 (IQR: 3–7), and the median antigen ratio was 18.72 (IQR: 3.04–66.09) (**Table 1**).

The participants with subarachnoid NCC had a longer illness duration (57 months, IQR: 14.5–142 versus 21 months, IQR: 9.5–72;  $p = 0.034$ ), stronger antibody responses on EITB (7, IQR: 7–7 versus 3, IQR: 2–5;  $p = 0.000$ ), and higher antigen ratios (63.50, IQR: 48.53–72.44 vs. 2.972, IQR: 1.35–6.20;  $p = 0.000$ ) than those with parenchymal NCC. Arachnoiditis presented only in the group with subarachnoid NCC (8, 29.63%).

There were 12 (22.64%) patients with cerebral hemodynamic changes suggesting vasculitis, with the most compromised vessel being the MCA in 11 (91.67%) (**Table 1**). These changes tended to be more frequent in the subarachnoid NCC group (9/29, 31.03% vs. 3/24, 12.50%;  $p = 0.187$ ), though this difference did not reach statistical significance. Subgroup analysis in individuals with subarachnoid NCC demonstrated more frequent signs of vasculitis in females (7/9, 77.8%, vs. 6/20, 30.0%,  $p = 0.041$ ), and a trend for more frequent arachnoiditis in individuals with signs of vasculitis on TCD (5/9 (55.56% vs. 3/20 (15.0%),  $p = 0.067$ ) (**Table 2**; **Supplementary Table S1**; <https://www.arquivosdeneuropsiquiatria.org/wp-content/uploads/2024/05/ANP-2023.0275-Supplementary-Material.docx>). Only in the group with parenchymal NCC, the 3 cases with signs of vasculitis were young females (ages 18, 21, and 27) (**Table 3**; **Supplementary Table S2**; online only). There were no differences in the frequency of vasculitis in TCD regarding the use of steroids, illness duration, and the results of the EITB and antigen-detection enzyme-linked immunosorbent assay (Ag-ELISA) (**Table 2**). Moreover, there was no difference in velocities between the subarachnoid and parenchymal NCC groups (**Table 4**).

## DISCUSSION

The NCC is a risk factor of stroke in young and middle-aged individuals.<sup>8</sup> Vasculitis occurs in this condition but is not

**Table 1** Characteristics of the participants

Characteristics		Total	Parenchymal NCC	Subarachnoid NCC	p-value
		n = 53 (%)	n = 24 (%)	n = 29 (%)	
Sex	Male	30 (56.60)	14 (58.33)	16 (55.17)	0.817
	Female	23 (43.40)	10 (41.67)	13 (44.83)	
Age (years)*		37 (29–48)	34 (27–47)	41 (31–50)	0.211
Schooling (years)*		11 (6–11)	11 (6–11)	10.5 (6–11)	0.215
Use of corticosteroids	Current	4 (9.09)	2 (11.76)	2 (7.41)	0.634
	Last 6 months	11 (25.58)	4 (25.0)	7 (25.0)	1.0
Illness duration (months)*		36 (12–120)	21 (9.5–72)	57 (14.5–142)	0.034
BMI (kg/m <sup>2</sup> )*		24.8 (22.89–26.8)	24.8 (22.9–26.2)	24.8 (22.9–27.3)	0.521
Western blot (bands)*		7 (3–7)	3 (2–5)	7 (7–7)	0.000
Antigen (ratio)*		18.7 (3.0–66.1)	2.97 (1.4–6.2)	63.50 (48.5–72.4)	0.000
Vasculitis according TCD		12 (22.64)	3 (12.50)	9 (31.03)	0.187
Arachnoiditis*		8 (15.09)	0 (0)	8 (27.59)	0.006
Compromised MCA		11 (91.67)	3 (100.0)	8 (88.89)	1.0

Abbreviations: BMI, body mass index; MCA, middle cerebral artery; NCC, neurocysticercosis; TCD, transcranial Doppler ultrasound.  
Note: \*Median (interquartile range).

always recognized, with a tendency to be more frequent in the subarachnoid type.<sup>10</sup> In this series, we demonstrated sonographic signs of vasculitis in 23% of the patients with NCC, supporting the utility of TCD in the diagnosis of NCC-related vasculopathy. The vasculopathy found in our group of patients was mostly MCA involvement in 11 cases (91.67%), concordant with previous reports. In 1998, Berrinagarrementeria et al. detected cerebral arteritis by angiography in 15/28 (53%) patients with subarachnoid NCC, 8 (53%) of whom had evidence of infarction on MRI, while in the group without arteritis only 1 had an infarction, and the most commonly affected vessels were the MCA and PCA.<sup>6</sup> The strong correlation between arteritis and stroke in these

patients suggests that early identification of CCV could allow the implementation of preventative measures, potentially decreasing morbidity and mortality. Tools such as TCD, a noninvasive and inexpensive diagnostic exam that can be performed at the bedside, can help in the diagnosis.<sup>13,17</sup>

Only one study has reported the use of TCD in the evaluation of intracranial arteries in NCC; the exam was performed on 9 patients with subarachnoid NCC and infarction, detecting large vessel arteritis in 7 of 10 arterial lesions demonstrated on cerebral angiography. The findings were occlusive in 2 and stenotic in 5. Furthermore, 4 of the 6 arterial lesions in the follow-up resolved in 3 cases when they were evaluated between 4 and 6 months of follow-up,

**Table 2** Factors associated to the presence of vasculitis according to TCD in patients with NCC

Variables		No vasculitis	Vasculitis	p-value
		n = 41 (%)	n = 12 (%)	
Sex	Male	28 (68.29)	2 (16.67)	0.002
	Female	13 (31.71)	10 (83.33)	
Age (years)*		39 (32–51)	31 (22.5–39)	0.002
Schooling (years)*		11 (6–11)	10 (7.5–11)	0.896
Use of corticosteroids	Current	4 (11.76)	0 (0)	0.559
	Last 6 months	9 (26.47)	2 (22.22)	1.0
Illness duration (months)*		24 (11.5–108)	54 (12–142)	0.272
BMI (kg/m <sup>2</sup> )*		24.9 (22.8–26.6)	24.8 (24.2–27.3)	0.558
Western blot (bands)*		7 (3–7)	7 (4.5–7)	0.562
Antigen (ratio)*		13.15 (3.0–62.8)	51.9 (25.7–76.9)	0.087
Arachnoiditis		3 (7.32)	5 (41.67)	0.010

Abbreviations: BMI, body mass index; NCC, neurocysticercosis; TCD, transcranial Doppler ultrasound.  
Note: \*Median (interquartile range).

**Table 3** Description of the cases of vasculitis

Age /Sex	Type of NCC	Cysts' location	WB*	Ag (ratio)	Stenosed artery	Velocities of the stenosed arteries (cm/s)	Arachnoiditis	Angioresonance
31/F	Subarachnoid	Suprasellar cistern, frontal interhemispheric fissure	7	50.3	Right MCA	PSV: 151; MV: 105	No	Variant of the inter-frontal configuration of the anterior circulation of the brain
23/F	Subarachnoid	Basal cisterns, sylvian fissure, right parietal convexity	7	93.0	Left ACA	PSV: 145; MV: 83	Yes	Normal
46/F	Subarachnoid	Right frontal superior sulcus, left sylvian fissure, corpus callosum	6	76.9	Right MCA	PSV:140; MV: 91	No	Normal
41/M	Subarachnoid	Basal, ambiens, preopontine, interpeduncular cisterns, sylvian fissure	7	72.4	Left MCA	PSV: 285; MV: 180	Yes	Stenosis of bilateral M1, bilateral anterior and posterior (predominantly left)
37/F	Subarachnoid	Basal cistern, interhemispheric fissure	7	48.5	Bilateral MCA, basilar artery	PSV: 196; MV: 136**	No	Stenosis of bilateral anterior A1 and bilateral MCA
48/F	Subarachnoid	Posterior horn right ventricle, ambiens, cerebellar cistern	7	82.0	Right MCA	PSV:148; MV: 103	No	Variant: fetal origin of the right PCA
22/F	Subarachnoid	Left sylvian fissure, calcarine fissure, parietal bilateral, ambiens, cerebellum	7	48.5	Left MCA	PSV: 144; MV: 95	Yes	Variant of the right ACA, hypoplasia of both the communicant arteries
31/M	Subarachnoid	Basal cistern	7	53.5	Left ACA	PSV: 139; MV: 81	Yes	Variant: absence of the right A1, right fetal PCA
36/F	Subarachnoid	Basal cisterns	7	76.9	Right MCA, bilateral ACA	PSV: 188; MV: 121***	Yes	Variant: absence of a part of the left M2
21/F	Parenchymal	Right frontal lobe	0	3	Right MCA	PSV: 155; MV: 95.	No	Normal
27/F	Parenchymal	Left parietal lobe	3	2.9	Right MCA	PSV: 140; MV: 84.	No	Variant: absence of the A1 segment
18/F	Parenchymal	Left parietal lobe	0	0.7	Right MCA	PSV:149; MV:95	No	Not performed

Abbreviations: ACA, anterior cerebral artery; Ag, antigen; BMI, body mass index; MCA, middle cerebral artery; MV, mean velocity; NCC, neurocysticercosis; PCA, posterior cerebral artery; PSV, peak systolic velocity; TCD, transcranial Doppler ultrasound; WB, Western blot.

Notes: \*Bands. \*\*The velocities described are of the most stenosed artery (left MCA). \*\*\*The velocities described are from the most stenosed artery (right MCA).

**Table 4** Average velocities of the arteries, according to the type of NCC

Characteristics		Parenchymal NCC Median (IQR)*	Subarachnoid NCC Median (IQR)*	p-value
Right MCA	PSV	92 (80.8–101.8)	100.5 (84–114.8)	0.181
	MFV	56.0 (49.6–64.2)	60.3 (50.9–75.8)	0.371
	PI	0.9 (0.8–0.9)	0.9 (0.8–1.1)	0.992
Left MCA	PSV	95 (81–107.5)	102.5 (84.5–117.5)	0.461
	MFV	58.86 (51.6–67.3)	62.27 (51.6–71.6)	0.504
	PI	0.93 (0.9–1.1)	0.90 (0.8–1.1)	0.351
Right ACA	PSV	83.25 (65–92.7)	80.5 (66.3–94.8)	0.983
	MFV	50.61 (41.1–56.7)	47.12 (39.5–60.4)	0.722
	PI	0.98 (0.9–1.1)	0.97 (0.9–1.1)	0.770
Left ACA	PSV	74.7 (60.7–87.3)	72 (60–94.8)	0.686
	MFV	45.8 (38.5–55.4)	47.4 (38.7–56.6)	0.957
	PI	0.9 (0.8–0.9)	0.9 (0.8–1.1)	0.491
Right PCA	PSV	49.3 (37–56.5)	49.67 (41.7–52)	0.703
	MFV	31.6 (22.5–36.2)	29.53 (25.9–33.1)	0.597
	PI	0.9 (0.8–1.1)	0.89 (0.7–1.1)	0.322
Left PCA	PSV	50 (39.7–62)	43.5 (39–53)	0.157
	MFV	31.75 (25.9–38.1)	25.86 (23.8–34.5)	0.111
	PI	0.86 (0.8–0.9)	0.87 (0.7–0.9)	0.947
Basilar artery	PSV	64.7 (55.7–75.2)	72.2 (56.8–77.7)	0.509
	MFV	42.3 (35.5–46.7)	42.4 (38.4–49.4)	0.458
	PI	0.90 (0.8–1.0)	0.93 (0.8–1.1)	0.686

Abbreviations: ACA, anterior cerebral artery; EDV, end diastolic velocity; IQR, interquartile range; MCA, middle cerebral artery; MFV, mean flow velocity; NCC, neurocysticercosis; PCA, posterior cerebral artery; PI, pulsatility index; PSV, peak systolic velocity.

Note: The velocities are measure in cm/s.

and in one case the stenosis remained at 12 months of evaluation. In the remaining 2 cases, the occlusive pattern remained until 18 months of follow-up.<sup>4</sup> The TCD is useful for diagnosis and could be useful for the follow-up, providing information about the progression of the arteriopathy and the risk of strokes in this population.

No patients with stroke were found in our study. However, sonographic signs of vasculitis were documented with a high frequency, which implies the presence of a risk factor in asymptomatic patients and, possibly, the opportunity to detect and prevent strokes. Vasculopathy in NCC more frequently affected those who had arachnoiditis, with approximately 50% previously reported in patients with arachnoiditis.<sup>6</sup>

The presence of vasculitis and subsequent strokes implies greater morbidity and mortality.<sup>4,8,18</sup> It is relevant to account for this entity, to take preventive measures, using tools such as the TCD for the evaluation of vascular compromise, to improve the diagnosis and management. Conventional techniques for neurovascular imaging can fail to distinguish between vessel wall diseases. Therefore, it is necessary to evaluate different diagnostic tools.<sup>19,20</sup>

The main limitation of this study was that TCD findings were not compared with an angiography, and we could not show the capacity of this tool for diagnosis. Additionally, the small sample size did not allow us to reach definite conclusions. The use of steroids was also a variable that could impact in the evaluation of vasculitis. However, in our study, there was no difference in this variable between the NCC and vasculitis groups.

In conclusion, our study showed that TCD can be used to evaluate cerebral hemodynamic changes, suggesting vasculitis in patients with NCC. Longitudinal follow-up studies must define the role of this exam in monitoring hemodynamic alterations, assessing the burden of stroke associated with CCV, and determining whether early detection of sonographic signs of this condition and subsequent preventative measures can reduce the risk of stroke in patients with NCC.

#### Authors' Contributions

DBI, JAB, HHG: conceptualization; SSB: data curation, formal analysis; DBI, HHG: funding acquisition, methodology; JAB, HHG: resources; JRQ, RE, IG, HS, JAB, HHG: supervision, validation; JAB, HHG: visualization; SSB,



HHG: writing of the original draft; SSB, DBI, JAB, RE, IG, HS, HHG: writing—review and editing. All authors have read and agreed to the published version of the manuscript.

#### Conflict of Interest

The authors have no conflict of interest to declare.

#### Acknowledgments

We would like to give thanks to the staff of the Cysticercosis Unit, Instituto Nacional de Ciencias Neurológicas, Lima, Peru, for the patient recruitment process.

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