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ORIGINAL RESEARCH

School-Based Epidemiology of *Schistosoma haematobium* Infection in Kharif District of Amran Governorate, North of Yemen: Need for Chemopreventive Strategy Revisiting

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Background: Urogenital schistosomiasis is a persistent public health problem in many rural areas of Yemen. Since 2014, *Schistosoma haematobium* epidemiology has not been assessed in Amran governorate, north of Yemen, where *S. haematobium* is known to be highly endemic. Therefore, this study determined the prevalence and risk factors associated with *S. haematobium* infection among schoolchildren in Kharif district of the governorate.

Methods: A cross-sectional survey was conducted among 529 schoolchildren aged 7 to 15 years in Kharif district. Data on children's demographics, clinical features, behaviors, and infection-related environmental factors were collected using a structured questionnaire. The urine filtration technique was used to detect and count *S. haematobium* eggs, and chemical reagent strips were used to detect microhematuria. The number of eggs per 10 mL of urine (EP10mL) was used to estimate the intensity of infection, which was classified as light (≤50 EP10mL) or heavy (>50 EP10mL). Multivariable binary logistic regression analysis was used to identify predictors of infection.

Results: Light-intensity *S. haematobium* infection was prevalent among 34.8% of schoolchildren in Kharif district, with a 95% confidence interval (CI) ranging from 30.7 to 38.8. Infection was significantly associated with microhematuria (P <0.001) and self-reported dysuria (P = 0.003). Family ownership of agricultural land was significantly associated with *S. haematobium* infection among schoolchildren [odds ratio (OR) = 1.8, 95% CI: 1.10–3.17; P = 0.030], which was further identified as an independent predictor of infection (adjusted OR = 2.2, 95% CI: 1.21–3.95; P = 0.010).

Conclusion: A considerable proportion of schoolchildren in Kharif district have light-intensity *S. haematobium* infections, mostly presenting with microhematuria and self-reported dysuria. The district's level of risk should be updated to moderate. Consequently, the chemopreventive strategy needs to be revisited to treat all school-age children biennially, regardless of enrollment status.

Keywords: *Schistosoma haematobium*, prevalence, risk factors, schoolchildren, Yemen

Introduction

Schistosomiasis is a poverty-related and neglected tropical disease that mainly affects impoverished rural communities in developing countries.[1,2] Six *Schistosoma* species cause human schistosomiasis, with *S. haematobium, S. mansoni* and *S. japonicum* being the most medically important.[3] According to 2021 estimates by the World Health Organization (WHO), over 251 million people worldwide were in need of preventive chemotherapy with praziquantel (PZQ) to reduce and prevent associated morbidity.[4] Various factors, including limited access to safe water, inadequate sanitation, engagement in agricultural activities and poor water contact practices, are linked to infection in rural areas.

Despite continuous prevention and control efforts in Yemen, schistosomiasis remains a major public health problem. The country launched a nationwide Schistosomiasis Control Project (SCP) in 2010,[5] aiming to reduce infection

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prevalence and intensity through mass drug administration (MDA) with PZQ. However, there have been reports of foci with high prevalence in endemic areas.[6–10] In 2014, nationwide schistosomiasis mapping among school-age children (SAC) revealed that infection rates with *Schistosoma* species exceeded the treatment threshold of ≥10% in approximately one-third of districts endemic for schistosomiasis.[10] It is estimated that more than 3.6 million individuals, including over 3 million SAC, required preventive chemotherapy in 2022.[11] However, nearly 2.9 million individuals received preventive chemotherapy with PZQ, including over 2.2 million SAC, achieving national coverage rates of 78.7% for all ages and 74.2% for SAC.[11]

Previously, in the late 1980s, *S. haematobium* infection was found to be prevalent among 28.9% of schoolchildren in Amran governorate, north of Sana'a, with *Bulinus* snails transmitting *S. haematobium* being more common than *Biomphalaria* snails that transmit *S. mansoni*.[12] In 2005, 58.9% of schoolchildren and the general population in Khamir district of Amran were found to be infected with *S. haematobium*.[13] After multiple rounds of school-based MDA with PZQ, the prevalence of *S. haematobium* infection among SAC in Kharif district dropped to 8.3%, as revealed by the nationwide mapping in 2014.[14] However, due to unrest in the country, the prevalence of infection among SAC in the district has not been updated since then, although infection prevalence is crucial in deciding whether to treat all at-risk individuals or only SAC and special risk groups.[15] Therefore, this study aimed to determine the prevalence and intensity of *S. haematobium* infection along with the identification of the associated risk factors among children enrolled in primary schools in Kharif district, Amran governorate.

Methods

Study Design, Population and Setting

A cross-sectional survey was conducted among schoolchildren aged 7 to 15 years in Kharif district in December 2021. The district is located in the southeastern part of Amran governorate (Figure 1), north of the capital city of Sana'a, at the coordinates 15°55′N 44°10′E. It spans an area of 264.8 km^2 and has a population of over 63,000 people,[16] with agriculture being the main activity of the population. Schistosomiasis is endemic in this district, most predominantly with *S. haematobium*.[13]

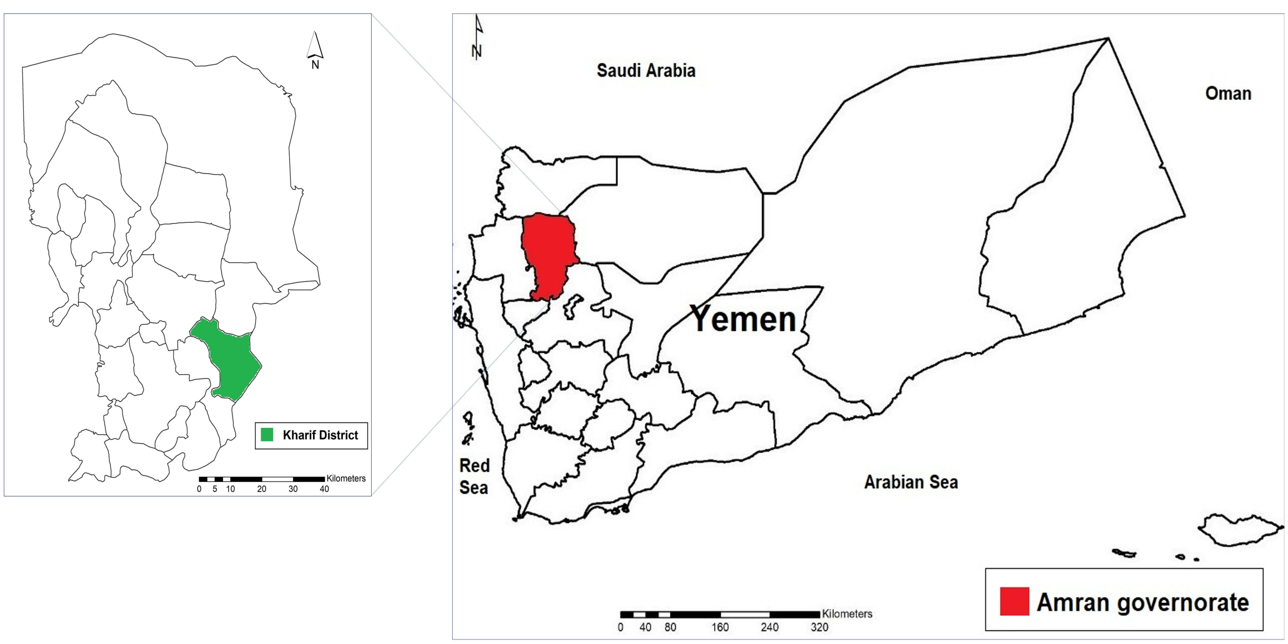

Figure 1 Map of Yemen showing the locations of Amran governorate and Kharif district.

Sample Size and Sampling Approach

A minimum sample size of 401 schoolchildren was determined using OpenEpi, version 3.01 (www.openepi.com). This calculation was based on an expected prevalence of 50% as a conservative approach, a confidence level of 95%, a precision of 6%, and a design effect of 1.5. However, to enhance the precision of the study's estimates, the sample size was increased to 529 children. A two-stage cluster sampling approach was employed, with schools serving as study clusters. First, six schools were selected at random from a compiled list of schools in the district. Second, children were randomly selected using systematic random sampling based on student records in the selected schools. In cases where a child refused to participate or was absent, they were replaced by the next child on the record.

Data Collection

Data on children's demographics, clinical features, behaviors, and environmental factors related to schistosomiasis were collected using a structured, reviewer-administered questionnaire. The questionnaire included questions on sociodemographic and clinical characteristics of children, source of drinking water, infection-related behaviors and environmental factors, as well as parasitological and laboratory results of urine examination.

Urine Collection and Examination

Children were instructed to collect urine samples in pre-labeled 20-mL screw-capped containers between 10 am and 2 pm. After collection, urine was visually inspected for hematuria and chemically tested for microhematuria using reagent strips (ACON Laboratories, San Diego, California, USA), according to the instructions provided by the manufacturer. The urine containers were then immediately transported to the laboratory of Dhibin Rural Hospital for parasitological examination. Urine samples were concentrated using the filtration technique and then examined for *S. haematobium* eggs under a light microscope.[17,18] The intensity of infection was determined by quantifying the number of eggs per 10 mL of urine (EP10mL),[17,18] which was then classified as light (≤50 EP10mL) or heavy (>50 EP10mL).[19]

Data Analysis

Data were analyzed using IBM SSPS Statistics, version 22.0 (IBM Corp., Armonk, NY, USA) at a significance level of <0.05. Categorical data were described using frequencies and percentages, while non-normally distributed continuous data were summarized using the median and interquartile range (IQR). The overall prevalence of *S. haematobium* infection was reported with a 95% confidence interval (CI). Subsequently, the classification based on WHO guidelines[20] was employed to ascertain the level of infection risk in the district. Briefly, the risk level was classified as low if the prevalence was ≥1% to <10%, moderate if the prevalence was ≥10% to <50%, and high if the prevalence was ≥50%.[20] The geometric mean egg count (GMEC) of *S. haematobium* was calculated and reported as EP10mL, along with its 95% CI. To test the association between *S. haematobium* infection and independent variables, univariate analysis was performed using Pearson's chi-square or Fisher's exact test, as appropriate, along with the odds ratios (ORs) and corresponding 95% CIs of associations. Then, multivariable binary logistic regression was used to identify independent predictors of infection, along with their adjusted ORs (AORs) and 95% CIs.

Ethical Considerations

This study complies with the ethical principles outlined in the Declaration of Helsinki concerning research involving human subjects. The Postgraduate Research Committee of the Faculty of Medicine and Health Sciences at Sana'a University reviewed and approved the study protocol. Following a clear explanation of the study purpose, written informed consent was obtained from the children's parents or legal representatives. In addition, children's assent to participate voluntarily was obtained. The confidentiality of participants and the privacy of their personal information were ensured.

Results

Study Population Characteristics

Most schoolchildren were males (84.5%), and more than half were older than 10 years, with a median age (IQR) of 11 (4) years. More than half of the children's households consisted of more than five members, with a median household size (IQR) of 6 (4) members. The fathers of most children were literate (73.9%) and unemployed (78.4%), while the mothers of most children were illiterate (76.6%) (Table 1).

Prevalence and Intensity of *S. haematobium* Infection

Infection with *S. haematobium* was prevalent among 34.8% (184/529; 95% CI: 30.7–38.8) of schoolchildren in Kharif district, corresponding to a moderate level of risk. For *S. haematobium* infections, the GMEC was 3.8 EP10mL (95% CI: 4.2–5.4). All infections exhibited a light intensity, ranging in EP10mL counts from 1 to 34.

Clinical Features Associated with *S. haematobium* Infection

Microhematuria (P <0.001) and self-reported dysuria (P = 0.003) were significantly associated with *S. haematobium* infection among schoolchildren. In contrast, neither macrohematuria nor pollakiuria was associated with the infection (Table 2).

Risk Factors Associated with *S. haematobium* Infection

Family ownership of agricultural land was significantly associated with *S. haematobium* infection among schoolchildren (OR = 1.8; 95% CI: 1.10–3.17; P = 0.030), which was further identified as an independent predictor of infection (AOR = 2.2, 95% CI: 1.21–3.95; P = 0.010). In contrast, *S. haematobium* infection showed no statistically significant association with gender, age, household size, parental literacy status, father's employment status, drinking water source, household sanitation facilities, or water contact-related activities (Table 3).

Table 1 Characteristics of Schoolchildren Enrolled in the Study*

Characteristics	n (%)
Gender	
Male	447 (84.5)
Female	82 (15.5)
Age (years)	
Median (IQR): 11 (4)	
>10	304 (57.5)
≤10	225 (42.5)
Household size (members)	
Median (IQR): 6 (4)	
≤ 5	223 (42.2)
> 5	306 (57.8)
Father's literacy status	
Literate	391 (73.9)
Illiterate	138 (26.1)
Father's employment status	
Employed	114 (21.6)
Unemployed	415 (78.4)
Mother's literacy status	
Literate	124 (23.4)
Illiterate	405 (76.6)

Note: *The total number included in the study was 529.
Abbreviation: IQR, interquartile range.

Table 2 Association of Clinical Features with *S. haematobium* Infection Among Schoolchildren in Kharif District, Amran Governorate, Yemen (2021)

Characteristics	N	*S. haematobium* Infection	
		n (%)	*P*-value
Macrohematuria			
Yes	66	25 (37.9)	0.332
No	463	159 (34.3)	
Microhematuria			
Positive	143	92 (64.3)	<0.001
Negative	386	92 (23.8)	
Pollakiuria			
Yes	234	81 (34.6)	0.508
No	295	103 (34.9)	
Dysuria			
Yes	97	46 (47.4)	
No	432	138 (31.9)	0.003

Abbreviations: N, number examined; n, number infected.

Table 3 Analysis of Risk Factors for *S. haematobium* Infection Among Schoolchildren in Kharif District, Amran Governorate, Yemen (2021)

Factors	N	*S. haematobium* Infection		*P*-value
		n (%)	OR (95% CI)	
Gender				
Male	447	151 (33.8)	Reference	
Female	82	33 (40.2)	1.3 (0.82–2.14)	0.259
Age (years)				
>10	304	107 (35.2)	Reference	
≤10	225	77 (34.2)	1.0 (0.67–1.38)	0.816
Household size (members)				
≤5	223	80 (35.6)	Reference	
>5	306	104 (34.0)	0.9 (0.64–1.32)	0.653
Father's literacy status				
Literate	77	27 (35.1)	Reference	
Illiterate	138	48 (34.8)	0.9 (0.55–1.77)	0.454
Father's employment status				
Employed	148	50 (33.8)	Reference	
Unemployed	381	134 (35.2)	1.0 (0.80–136)	0.764
Mother's literacy status				
Literate	124	40 (32.3)	Reference	
Illiterate	405	144 (35.6)	1.1 (0.83–1.47)	0.500
Family ownership of agricultural land				
No	79	19 (24.1)	Reference	
Yes	450	165 (36.7)	1.8 (1.10–3.17)	0.030*
Source of drinking water				
Tanker trucks	127	37 (29.1)	Reference	
Rainwater harvesting	79	27 (34.2)	1.3 (0.69–2.31)	0.447
Wells	323	120 (37.2)	1.4 (0.92–2.24)	0.109

(*Continued*)

Table 3 (Continued).

Factors	N	*S. haematobium* Infection		*P*-value
		n (%)	OR (95% CI)	
Household sanitation facilities				
Flush or pour flush into pit latrines	370	128 (34.6)	Reference	
Flush or pour flush into open areas	159	56 (35.2)	1.0 (0.70–1.52)	0.890
Swimming or bathing in ponds or valleys				
No	78	34 (43.6)	Reference	
Yes	451	150 (33.3)	0.7 (0.40–1.05)	0.077
Washing clothes in ponds or valleys				
No	226	88 (38.9)	Reference	
Yes	303	96 (31.7)	0.7 (0.51–1.04)	0.051
Carrying water from valley to house				
No	281	105 (37.4)	Reference	
Yes	247	78 (31.6)	0.8 (0.54–1.11)	0.096

Notes: *Confirmed as an independent predictor of *S. haematobium* infection using multivariable binary logistic regression (AOR = 2.2, 95% CI = 1.21–3.95; *P* = 0.010).
Abbreviations: N, number examined; n, number infected; OR, odds ratio; CI, confidence interval.

Discussion

The overall prevalence of *S. haematobium* infection among schoolchildren in Kharif district after repeated rounds of MDA was 34.8%, which was significantly associated with microhematuria and self-reported dysuria. Schoolchildren belonging to families that own agricultural land showed significantly higher odds of infection compared to their counterparts, with family ownership of agricultural land being identified as an independent predictor of infection using multivariable binary logistic regression.

The prevalence of *S. haematobium* infection among schoolchildren in the present study indicates a moderate level of infection risk, as outlined by WHO guidelines.[20] In contrast, the 2014 mapping revealed a low level of infection risk in the district, with only 8.3% of children found to be infected with *S. haematobium*.[14] In comparison, lower *S. haematobium* infection rates were reported in five Yemeni governorates (23.8%),[7] Abyan governorate in the south (18%),[21] Taiz governorate in the southwest (7.4%),[22] as well as Hajjah and Sadah governorates in the north (1.7% and 3.3%, respectively).[23,24] Nevertheless, a higher prevalence of 58.9% was documented in the neighboring Khamir district of the same governorate in 2005.[13] Notably, all schoolchildren in the present study had light-intensity infections, which may be due to the repeated rounds of MDA against schistosomiasis under the SCP since 2010.[5] In contrast, 87.9% of Nigerian SAC were found to have heavy-intensity *S. haematobium* infections despite ongoing administration of PZQ.[25] It is worth noting that even light-intensity infections can cause subtle morbidities, including growth retardation, anemia, and cognitive impairment.[26–28]

The high prevalence of *S. haematobium* in this study is most likely attributed to frequent reinfections in the district, as PZQ does not prevent infection with schistosomes and is ineffective against juvenile schistosomes.[29] Post-MDA reinfection with *S. haematobium* has been documented in several African countries.[30–36] Various factors have been identified as predictors of reinfection, including age,[31,37–39] prevalence and intensity of infection before chemotherapy,[30,34,40] incomplete treatment,[31] and proximity to water bodies.[41] Furthermore, changes in socioeconomic conditions resulting from armed conflicts and humanitarian crises in Yemen could contribute to *S. haematobium* transmission in endemic districts, including Kharif. Moreover, the country is among the least developed countries, and its ranking in terms of development and access to basic services has declined in recent years. The United Nations ranked the country 183 out of 191 countries and territories in 2021–2022, compared to 158 in 2012.[42] As a result, increased poverty, inadequate sanitation, limited access to safe water, and deteriorated healthcare services may contribute to *S. haematobium* transmission in endemic areas of the country.

The control strategy for *S. haematobium* infection in Kharif district needs to be adjusted due to the transition of transmission risk from low to moderate. The approach recommended by WHO is to provide enrolled and non-enrolled SAC with preventive chemotherapy once every two years, rather than providing it twice during their primary school years.[20] By expanding treatment to enrolled and non-enrolled SAC, control efforts aim to reach a larger proportion of the affected population and reduce the overall disease burden. However, it is important to recognize that the use of MDA alone may not be sufficient to effectively interrupt transmission, as the present findings suggest. While MDA is a key component in reducing schistosomiasis prevalence and intensity, the changing epidemiology highlights the need for additional interventions to complement MDA efforts. Integration of such interventions may help address the factors contributing to the changing epidemiology of *S. haematobium* infection. These interventions may include provision of safe water, improved sanitation, snail control, and health education.

The significant association between microhematuria, but not macrohematuria, and *S. haematobium* infection in the present study could be possibly explained by the fact that the intensity of all infections among children in this study was light. Such a significant association is consistent with findings in several endemic countries.[43–48] The WHO Expert Committee on the Control of Schistosomiasis emphasized the utility of microhematuria for determining prevalence, identifying infected people, and assessing the effectiveness of interventions.[49] A study in a southern Yemeni village showed high sensitivity (92.9%) and specificity (94%) of reagent strips in diagnosing *S. haematobium* infection in schoolchildren.[21] However, reagent strip sensitivity in communities with light infections is questionable.[50] This study also found that self-reported dysuria was significantly associated with *S. haematobium* infection, aligning with previous findings in Yemen and elsewhere.[21,51,52] Using a combination of morbidity markers, such as hematuria and dysuria, can be more effective for rapid diagnosis and mapping of *S. haematobium* infection.[53] However, further investigation is required to assess the utility of this approach in the study district.

The significantly higher infection rate with *S. haematobium* among schoolchildren from families that owned agricultural land, which was further confirmed as an independent predictor of infection, could be attributed to the fact that children are engaged in irrigated agriculture and are therefore more exposed to the infection. Accordingly, even with repeated rounds of MDA with PZQ, environmental and occupational factors could still play an important role in reinfection and contribute to sustained transmission. Therefore, it is crucial to consider these factors when revisiting the MDA strategy in the study district. Household engagement in irrigated agriculture has been shown to be significantly associated with a higher risk of infection with *S. haematobium*.[54] Paternal occupation as a farmer has also been identified as a predictor of *S. haematobium* infection in schoolchildren.[55,56] The absence of association between other types of water contact activities and *S. haematobium* infection in this study contradicts findings reported among schoolchildren in Yemen[57,58] and elsewhere.[59–61] Nevertheless, this finding is consistent with that reported in coastal Kenya.[31] On the other hand, the number of household residents was not associated with a higher risk of infection with *S. haematobium* among children in the present study. Likewise, family size did not show a significant association with schistosomiasis among rural children in Yemen.[7]

Females in the present study showed a higher rate of *S. haematobium* infection compared to males, but gender was not significantly associated with the risk of infection. This finding aligns with previous ones among children in Yemen and elsewhere.[7,22,62] However, other reports have identified male gender as a predictor of infection.[55,57,58,60,63] The discrepancy between the present study and previous findings may be explained by the underrepresentation of female students, who accounted for only 15% of the participants, probably due to the lower enrollment rate of girls in rural districts of the country. Schoolchildren's age also did not show a significant association with infection in the present study, which contrasts with findings from districts in other Yemeni governorates,[7] where schistosomiasis was significantly more frequent in older children. On the other hand, the present study found no significant association between parental illiteracy and *S. haematobium* infection, which is consistent with a finding among schoolchildren in Ibb governorate.[57] In contrast, fathers' illiteracy was significantly, although not independently, associated with schistosomiasis in rural communities in five Yemeni governorates.[7] The absence of a significant association between fathers' employment status and *S. haematobium* infection among their children in the present study is consistent with a finding reported for rural children in five Yemeni governorates.[7] In the present study, household water sources and sanitation facilities were not significantly associated with *S. haematobium* infection, which agrees with a finding among schoolchildren in Ibb governorate.[57] In contrast, the use of unsafe drinking water sources was identified as an independent predictor of schistosomiasis among rural children from other districts in five Yemeni governorates.[7] Differences in the contamination levels of water sources and the quality of sanitation facilities across areas of the country could contribute to these different associations.

The present study provides valuable insights into the transition of *S. haematobium* infection risk in the study district from low to moderate. Nevertheless, a few limitations should be acknowledged and considered when interpreting its findings. Due to logistic constraints, the study was conducted among enrolled SAC only, potentially introducing selection bias. The study missed capturing data from non-enrolled children, who may have different socioeconomic backgrounds, living conditions and infection-related behaviors compared to enrolled children. Consequently, certain subgroups that could be at a higher risk of infection might be underrepresented, including those from disadvantaged backgrounds. To improve generalizability, a larger sample size than originally required was used to enhance precision in estimating prevalence and associations by narrowing CIs around their estimates. However, it is important to exercise caution when generalizing the study findings to the broader population of children in the district. In addition, future studies involving both enrolled and non-enrolled SAC are recommended to gain a more comprehensive understanding of *S. haematobium* epidemiology. On the other hand, recall bias might be introduced when collecting self-reported data on clinical features and infection-related behaviors, possibly leading to inaccuracies in recall or reporting by schoolchildren.

Conclusion

A considerable proportion of schoolchildren in Kharif district have light-intensity *S. haematobium* infections, mostly presenting with microhematuria and self-reported dysuria. The district's level of risk, which was previously classified as low in 2014, should be updated to moderate. Consequently, the chemopreventive control strategy needs to be revised to treat all school-age children, regardless of enrollment status, biennially. Ownership of agricultural land by children's families can serve as an independent predictor of their likelihood of being infected with *S. haematobium*.

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Disclosure

The authors report no conflicts of interest in this work.

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