

Burden of tuberculosis in Kampala, Uganda

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Objective To determine the prevalence and incidence of tuberculosis in one of Uganda's poor peri-urban areas.

Methods Multi-stage sampling was used to select a sample of households whose members were evaluated for presence of signs and/or symptoms of active tuberculosis; history of tuberculosis treatment; and relevant demographic, socioeconomic, and household environment characteristics. Patients with suspected tuberculosis underwent standardized evaluation for active disease.

Findings A sample of 263 households with 1142 individuals was evaluated. Nineteen people were classified as having had tuberculosis during the one-year reference period (May 2001–April 2002): nine (47%) cases already had been diagnosed through the health care system, while 10 cases (53%) were diagnosed through the survey. The prevalences for all forms of tuberculosis and for sputum smear-positive tuberculosis were 14.0 (95% confidence interval (CI) 7.8–20.3) and 4.4 (CI = 0.83–7.89) per thousand, respectively. The incidences for all forms of tuberculosis and for sputum smear-positive tuberculosis were 9.2 (CI = 3.97–14.4) and 3.7 (CI = 0.39–6.95) per thousand per year, respectively.

Conclusion The rate of tuberculosis in this peri-urban community was exceptionally high and may be underestimated by current surveillance systems. The need for interventions aimed at reducing tuberculosis transmission in this, and other similar communities with high case rates, is urgent.

Keywords Tuberculosis, Pulmonary/epidemiology; Households; Cross-sectional studies; Cohort studies; Sampling studies; Uganda (source: MeSH, NLM).

Mots clés Tuberculose pulmonaire/épidémiologie; Ménages; Etude section efficace; Etude cohorte; Etude échantillon; Ouganda (source: MeSH, INSERM).

Palabras clave Tuberculosis pulmonar/epidemiología; Hogares; Estudios transversales; Estudios de cohortes; Muestreo; Uganda (fuente: DeCS, BIREME).

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Introduction

Over the past two decades, the number of tuberculosis cases has risen worldwide, especially in the developing countries of south-east Asia and sub-Saharan Africa, where co-infection with human immunodeficiency virus (HIV) and tuberculosis is common (1, 2). Case notification data often are used to assess the burden of tuberculosis. The wide belief, however, is that a substantial number of cases of tuberculosis are not detected by the health care systems in most of these countries (3, 4), and surveys of the prevalence of tuberculosis in some of these countries support this belief (5, 6). Furthermore, the poor peri-urban areas of developing countries, where living conditions are unsatisfactory with overcrowding, poor hygiene and inadequate sanitation, are usually most affected by tuberculosis (7, 8). Such living conditions, coupled with high prevalence of HIV infection and lack of access to health care and/or poor health-seeking behavior (8, 9), may lead to a vicious circle of transmission of

diseases, including tuberculosis. National average notification data often do not reveal the overwhelming burden of tuberculosis in these settings.

Like most of sub-Saharan Africa, Uganda has a high prevalence of HIV (10–12) and tuberculosis infection (13, 14). Health care managers and tuberculosis control authorities in the country believe that the prevalence of the disease is much higher than revealed by notification figures because of underreporting and due to poor access to health care. Most of the cases are believed to occur in poor peri-urban areas of the country characterized by high population density, and poor housing and living conditions. No reliable information about the true burden of tuberculosis in these areas exists, however. Rational strategies for control of tuberculosis need a sound knowledge of the magnitude of the burden of the disease (15). We conducted a survey in Kawempe division, a peri-urban part of Kampala (the capital city of Uganda), to determine the prevalence and incidence of tuberculosis in this community.

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Materials and methods

Setting and sample selection

Kawempe division is one of the five administrative divisions of Kampala city, covers an area of approximately 30 km², and has an estimated population of 245 015 inhabitants (16). It is composed of 18 parishes, each made up of 3–7 villages. The district is also home to Mulago Hospital and two public health care clinics. Mulago Hospital tuberculosis clinic is a referral treatment centre for this division and the country.

A sample of households from Kawempe division was surveyed in July 2001–April 2002 to identify individuals with signs and symptoms of tuberculosis; history of tuberculosis treatment; and relevant demographic, socioeconomic, and household environment characteristics. Crowding increases the risk of transmission of *Mycobacterium tuberculosis* (17, 18), so population density was used as an index for crowding to maximize representativeness of participants from areas of different crowding levels during selection of the study sample with a two-stage stratified cluster sampling procedure (19). The 18 parishes were first stratified into seven strata based on the seven population densities established by the 1991 population census (16). Stage I of the sampling involved random selection of one parish from each of the seven strata (seven parishes selected at stage I). Stage II involved random selection of a sample of households from each of the seven parishes. This was achieved by using a map of the parish to identify road junctions in the parish and then selecting a random sample of junctions. From each of these junctions, a random direction was chosen and trained home health visitors moved from house to house to identify eligible consenting households until the number of households allocated to that parish was reached. The total sample of households allocated to each stratum was proportional to the total population in that stratum. A household was defined as a group of individuals living within one domicile, who normally shared meals together. A household member was defined as an individual who had spent at least 14 consecutive days in the domicile over the three months before the household was identified by the study team. The institutional review boards of Uganda's National Council for Science and Technology and the University Hospitals of Cleveland, Ohio, approved the study.

Measurements

To evaluate the household members, the home health visitors explained the purpose of the study to the most responsible adult person present at the time of the visit. They also provided health education to the household members about tuberculosis. Written informed consent was obtained from the head of the household, each adult person, and parents or guardians of children in the household aged <18 years. The home health visitors then evaluated all eligible household members with a standardized questionnaire. The questionnaire collected information on relevant social and demographic characteristics of each individual, presence of signs or symptoms of tuberculosis, history of tuberculosis treatment, bacille calmette–Guérin (BCG) vaccination status, and known current or past contact with a tuberculosis case. Vaccination with BCG was determined through the presence or absence of a BCG scar. Home health visitors also evaluated the household environment, including the number of people in the household and the number of windows, rooms and types of room in the domicile.

An individual was suspected of having tuberculosis if they reported having hemoptysis over the preceding three weeks or had experienced at least two specific signs and symptoms over the preceding three weeks (Box 1). All tuberculosis suspects were referred to Mulago Hospital Tuberculosis Treatment Center, where a medical officer completed a work-up for active tuberculosis that included a detailed medical evaluation, sputum microscopic examination, mycobacterial culture, and a chest X-ray radiograph. Postero-anterior chest radiographs were taken for all people with suspected tuberculosis and were interpreted by two doctors experienced in the diagnosis and management of tuberculosis. The extent of disease on X-ray was graded on a four-category ordinal scale as normal, minimal, moderately advanced, and far advanced. Three sputum samples were taken from each person with suspected tuberculosis — one spot specimen and two early morning specimens. Gastric aspirates were performed in children with symptoms of active disease or abnormalities on chest X-ray that did not improve with a trial of antibiotic therapy. Participants who were taking tuberculosis treatment at the time of interview and those who had ever had tuberculosis were asked to provide details about their treatment, including date treatment started, date treatment was finished, specimen microscopy, and mycobacterial culture results, if any. A diagnosis of tuberculosis was verified with a tuberculosis treatment card issued by the National Tuberculosis and Leprosy Control Programme (NTLCP) or with medical records when available.

In order to follow-up study participants for occurrence of tuberculosis over the study reference period (May 2001–April 2002), the recall period for details on history of active tuberculosis was extended back to May 2001 during the home interviews, and respondents were asked to report to the study clinic if they developed any illness after the interview. Participants who reported subsequently to the study clinic were evaluated for active tuberculosis or were referred to appropriate health care clinics if tuberculosis was definitely not suspected. All confirmed tuberculosis cases were notified to the NTLCP and were treated with self-administered, standard, short-course, antituberculosis chemotherapy, according to tuberculosis treatment guidelines in Uganda (20).

Classification of tuberculosis cases

Two doctors independently classified participants with suspected tuberculosis based on clinical, radiographic, and microbiological findings according to the following definitions: definite tuberculosis (culture confirmed), probable tuberculosis (smear-positive and clinical presentation consistent with tuberculosis or moderate chest X-ray abnormality and objective

Box 1. Signs and symptoms suggestive of tuberculosis

A person was suspected of having tuberculosis if over the preceding three weeks they reported having hemoptysis or had experienced at least two of the following signs and symptoms:

- cough lasting more than two weeks
- unintentional weight loss
- loss of appetite
- swelling of glands
- night fevers
- drenching night sweats

evidence of response to antituberculosis treatment), possible tuberculosis (clinical presentation consistent with tuberculosis), or unlikely tuberculosis (21). Response to therapy was evaluated by improvement of radiographic abnormalities and weight gain with antituberculosis therapy. Where the two doctor's classifications differed, they met to reach a consensus classification.

Statistical analysis

Statistical analysis focused on estimating the prevalence and incidence of tuberculosis in the study population. In this analysis, tuberculosis cases were participants with suspected tuberculosis who were classified as having definite or probable tuberculosis. A "prevalent case" was an individual determined to have been a tuberculosis patient at any time during the reference period, irrespective of whether diagnosis was made before or after May 2001. A tuberculosis case also was defined as an incident case, if diagnosis was made as a new episode of tuberculosis within the study reference period. The prevalence and incidence of tuberculosis were calculated per 1000 people, taking into consideration the stratified cluster sampling procedure used to select the sample (19). They were calculated as follows:

$$\text{Prevalence/incidence} = \left(\sum_{h=1}^H N_h \bar{y}_h / N \right) * 1000$$

N_h = number of households within the hth stratum,

$$\bar{y}_h = \sum_{i=1}^{n_h} y_{hi} / n_h, \sum_{i=1}^{n_h} y_{hi} = \text{total number tuberculosis}$$

cases in the hth stratum, $y_{hi} = 1$, if the ith individual from the hth stratum is a tuberculosis case, or 0 otherwise, n_h = number of households selected from the hth stratum, and N = estimated number of people in study population (16).

The variance of the prevalence/incidence estimate was calculated as:

$$\text{Var}(\text{prevalence/incidence}) = \frac{1}{(N/1000)^2} \sum_{h=1}^H N_h \left(\frac{N_h - n_h}{a_h - 1} \right) \left[\frac{1}{(a_h - 1)b_h^2} \left(\sum_{i=1}^a y_{hi}^2 - \frac{y_h^2}{a_h} \right) \right]$$

a_h = number of households selected from the hth stratum and b_h = average household size in the hth stratum

Results

Characteristics of participants and their housing conditions

A total of 263 households containing 1142 individuals was surveyed. Most participants (731, 64%) were female, and 563 (49%) were aged <16 years. The mean age was 18.1 (SD 15.2) years. The educational level of most participants was low, as most (822, 72%) had attained only primary level education. Overall, 160 (14%) of the participants reported having come into contact with someone they believed had tuberculosis within the 30 days before the interview.

The median household size was five people, and most households (190, 73%) were composed of more than three people (Table 1). The households were crowded, with 3.2 people per room on average. The rooms were also poorly ventilated, with 0.6 windows per room and five people per window on average. In total, 29 (11%) households reported doing most of their cooking in the house with charcoal, and 237 (90%)

households shared their toilet or latrine with at least one other household. No significant differences were found in the housing conditions between the parishes.

Active tuberculosis cases

In total, 19 participants were classified as having had definite or probable tuberculosis during the one-year study reference period; this included 12 incident cases. Nine (47%) of these cases were already diagnosed through the health care system, but 10 (53%) cases were diagnosed through our study. Of the nine cases already diagnosed, one had smear-positive sputum and one case had sputum that was culture-positive for tuberculosis. Of the 10 cases diagnosed through our study, eight were diagnosed among participants suspected of tuberculosis during the home interviews (five with smear-positive sputum and six with sputum that was culture-positive for tuberculosis); the remaining two cases were diagnosed among participants who developed illness after the home interviews and subsequently reported to the study clinic as advised. Table 2 shows the distribution of the cases by stratum.

The average age of the 19 cases was 23 (SD 13) years; six (32%) cases were aged <15 years, 13 (68%) were female, and nine (48%) had a BCG vaccination scar. No significant difference was seen in the distribution of cases by sex, BCG vaccination

Table 1. Characteristics of households

Characteristic	Summary measure
Total number of households	263
<i>Family size</i>	
1–3 people	73 (28) ^a
4–5 people	112 (43) ^a
≥6 people	78 (30) ^a
Median (range)	5 (1–22) ^b
<i>Type of residence</i>	
"Muzigo" with inner walls not reaching ceiling	36 (14) ^a
"Muzigo" with inner walls reaching ceiling	168 (64) ^a
Single family house	56 (21) ^a
Other	3 (1) ^a
<i>Indices of crowding and ventilation</i>	
People per habitable room	
Mean	3.2 (1.7) ^c
Median	3.0 (0.6–11) ^b
Windows per habitable room	
Mean	0.6 (0.5) ^c
Median	0.5 (0–4) ^b
Windows per person	
Mean	0.2 (0.3) ^c
Median	0.2 (0–1.5) ^b
<i>In-house cooking</i>	
Firewood or charcoal	30 (11) ^a
Electricity	7 (3) ^a
<i>Household amenities</i>	
Potable water inside household	183 (70) ^a
Electricity inside household	129 (49) ^a
Family use of own toilet or latrine	26 (10) ^a

^a Numbers in parentheses are percentages.

^b Numbers in parentheses are ranges.

^c Numbers in parentheses are standard deviations.

Table 2. Prevalence of tuberculosis by stratum

Population density (persons/km ²)	Stratum		Sample		Prevalent Cases
	Estimated Population	Estimated number of households	No. of households	No. of people	
≥17 000	22 112	4422	39	136	3
13 000–16 999	56 742	11 348	51	250	1
9000–12 999	47 444	9489	56	225	4
6000–8999	23 522	4704	23	106	1
4000–5999	36 948	7390	33	169	3
2000–3999	44 835	8967	49	193	6
0–1999	13 411	2682	12	63	1
Total	245 015	49 003	263	1142	19

status, or age, although a relatively higher proportion of cases were diagnosed in the age group 16–25 years (Table 3). Cases were more likely to come from households with three or more people per room, but this difference did not attain statistical significance ($P = 0.061$). No difference was found in the distribution of cases by other living domicile condition indices, including number of windows per room and number of persons per window.

Of the 11 cases with sputum culture testing, eight (73%) had positive results. Of the nine cases with chest X-ray radiographs, five (56%) had advanced disease on chest X-ray, two (22%) had minimal disease, and two had normal X-rays. Five of these cases (56%) had cavitory disease (Table 4).

Prevalence and incidence estimates

Overall, six of the 19 prevalent cases had sputum that was smear-positive for tuberculosis. The prevalence of all forms of tuberculosis therefore was calculated to be 14.0 (CI = 7.81–20.3) cases per 1000 people, and the prevalence of smear-positive pulmonary tuberculosis was 4.4 (CI = 0.83–7.89) cases per 1000 people. Five of the 12 incident cases had sputum that was smear-positive for tuberculosis. The incidence of all forms of tuberculosis thus was calculated to be 9.2 (CI = 3.97–14.4) cases per 1000 people per year, and the incidence of smear-positive pulmonary tuberculosis was 3.7 (CI = 0.39–6.95) cases per 1000 people per year.

Discussion

Although health care professionals in Uganda acknowledge that tuberculosis case rates in the poor peri-urban communities of the country are higher than those in the rest of the country, the magnitude of the disease in these communities has been unknown. This is the first systematic study conducted to quantify tuberculosis case rates in the poor peri-urban parts of Kampala city. Our findings reveal exceptionally high case rates of 9.2 new cases per 1000 people per year, which is nearly five times the estimated national average of two new cases per 1000 people per year (1, 22). These findings support the assertion that national average notification figures often may not reveal the disparity in case rates between the poor urban and other parts of the country. The high case rates in this community suggest high levels of transmission of tuberculosis that are likely to be enhanced by the bad living conditions (including poorly ventilated and crowded domiciles), as well as a high prevalence of HIV infection in this community, which is estimated at 10% (11). The public health implication of these findings is

that in the absence of any intervention, high case rates are likely to continue. Although ongoing national efforts to reduce the prevalence of HIV infection continue — and will reduce case rates of HIV-associated tuberculosis — extra efforts are needed to control tuberculosis transmission in the poor peri-urban parts of the country. These parts of the country probably contribute the bulk of cases in the country.

Findings from this study also suggest that some of the prevailing cases are not detected at all or that delays in detection are substantial. Out of the 17 prevailing cases found at the time of home interviews, eight (47%) cases had not yet been detected by the health care system, including five cases with smear-positive pulmonary tuberculosis and five with cavitory disease — a sign of late and advanced disease (23). Further suggestion of underdetection is supported by the fact that notification figures to the NTLCP for 1998 estimate the annual prevalence of tuberculosis in Kampala city as 7.6 cases per 1000 people (22), which is only 54% of the prevalence of 14 cases per 1000 people established by our study. This study was conducted in only one of the five divisions of the city and in a different calendar year, but this may not account for the large difference between the case notification rate and the survey estimate. Underestimation of the burden of tuberculosis may lead to inadequate allocation of resources to schemes aimed at control of transmission. Accurate estimates of the magnitude of tuberculosis are a prerequisite for rational tuberculosis control planning (15). Furthermore, although it is possible that some of the eight undetected cases would eventually have sought medical care and treatment, such cases may go undetected for weeks or months. They continue to expose the family and other members in the community to tuberculosis infection, thus propagating transmission. This is particularly worrying given the long duration of infectiousness implied by our findings. The estimated incidence and prevalence of sputum smear-positive tuberculosis and relation with duration of infectiousness (24) mean that the estimated duration of infectiousness of a tuberculosis case in this community is approximately 1.2 years. Early detection of tuberculosis cases needs to be improved, so that treatment is initiated early to minimize pre-treatment transmission in the community (25, 26).

Although expensive, active case-finding in communities with a high prevalence of tuberculosis could prove cost effective in the long run, as a result of prevented new infections. Intensified health education about tuberculosis transmission and disease recognition could also prove rewarding. Health education

Table 3. Distribution of tuberculosis cases by demographic and household characteristics

Characteristic	Total people	Cases of tuberculosis	P-value
<i>Demographic</i>			
Age (years)			
0–5	275	3 (1.1) ^a	0.626
6–15	288	3 (1.0)	
16–25	304	7 (2.3)	
26–35	157	3 (1.9)	
≥35	118	3 (2.5)	
Sex			
Men	411	6 (1.5)	0.444
Women	731	13 (1.91.8)	
Bacille Calmette–Guérin scar			
Absent	430	10 (2.3)	0.132
Present	712	9 (1.3)	
<i>Household</i>			
People per room			
<3	109	4 (3.7)	0.061
≥3	154	15 (9.7)	
Windows per room			
<0.5	126	9 (7.1)	0.961
≥0.5	137	10 (7.3)	
Windows per person			
<0.2	116	5 (4.3)	0.105
≥0.2	147	14 (9.5)	

^a Numbers in parentheses are percentages.

has played a significant role in the fight against HIV infection in Uganda (27), and similar efforts could be used against tuberculosis.

Study limitations

This study has three important limitations. First, we did not assess risk factors for tuberculosis in this setting; therefore, the main determinants of tuberculosis in this community are unclear. Such information is important for designing appropriate interventions, as well as for generalizability considerations. A recent study in Kampala city, however, described the determinants of tuberculosis in household contacts of sputum smear-positive tuberculosis cases (28), and we believe that the results from that study are relevant to this community. Second, we were unable to subject all tuberculosis cases to the same diagnostic evaluation and classification, as some of them had already been diagnosed through the health care system by the time of the home interviews. This may have resulted in overdiagnosis of cases, so that we may have overestimated the prevalence and incidence of tuberculosis in this community. Third, this study involved a small sample size of 1142 participants, which is only 0.5% of the reference population. This explains the wide confidence intervals for the estimates reported and implies that the results are not as precise as might be desired.

Conclusion

The burden of tuberculosis in this setting is exceptionally high and may be underestimated by current surveillance systems.

Table 4. Clinical characteristics of the tuberculosis cases

Characteristic	Cases
<i>Smear grade</i>	
Negative	13 (68) ^a
+ 0 (0)	
++	1 (5)
+++	5 (26)
Total	19
<i>Culture</i>	
Negative	3 (27)
Positive	8 (73)
Total	11
<i>Culture and smear</i>	
Smear-negative; culture-negative	3 (27)
Smear-positive; culture-negative	0 (0)
Smear-negative; culture-positive	2 (18)
Smear-positive; culture-positive	6 (55)
Total	11
<i>X-ray results</i>	
Extent of disease	
Normal	2 (22)
Minimal	2 (22)
Advanced	5 (56)
Cavitation	5 (56)
Total	9

^a Numbers in parentheses are percentages.

At any one time, undetected cases of infectious tuberculosis in this community propagate infection. Strategies for tuberculosis case detection need to be improved urgently in order to minimize transmission. Public health officials should intensify health education efforts aimed at promoting health-seeking behaviour to facilitate early case detection. Furthermore, active case-finding and household contact investigations may prove to be a valuable and cost-effective tuberculosis control strategy in this and other communities with high case rates. ■

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Conflicts of interest: none declared.

Résumé

Charge de la tuberculose à Kampala (Ouganda)

Objectif Déterminer la prévalence et l'incidence de la tuberculose dans l'une des zones péri-urbaines défavorisées de Kampala.

Méthodes Echantillonnage à plusieurs degrés pour sélectionner des foyers où l'on a recherché des symptômes de tuberculose évolutive, étudié les antécédents de traitement antituberculeux, de même que les caractéristiques démographiques, socio-économiques et l'environnement de chacun de ces foyers. En cas de suspicion de tuberculose, on a procédé à une évaluation standardisée des patients.

Résultats L'étude a porté sur un échantillon de 263 foyers rassemblant 1 142 personnes et a classé dix-neuf d'entre elles dans la catégorie des sujets atteints de tuberculose pendant les 12 mois de référence (mai 2001 - avril 2002). Le système de santé

avait déjà posé le diagnostic pour neuf des cas (47 %) et l'étude a permis de diagnostiquer les 10 autres (53 %). La prévalence était de 14,0 (intervalle de confiance (IC) à 95 % : 7,8 - 20,3) pour la tuberculose en général, toutes formes confondues, et de 4,4 (IC : 0,83-7,89) pour 1 000 pour la tuberculose à frottis positif. Pour l'incidence, les chiffres correspondants sont de 9,2 (IC : 3,97-14,4) et de 3,7 (IC : 0,39-6,95) pour 1 000 et par an.

Conclusion Dans cette communauté péri-urbaine, la fréquence de la tuberculose est exceptionnellement élevée et elle est peut-être sous-estimée par les systèmes de surveillance actuels. Il est donc urgent d'intervenir afin de lutter contre la transmission dans cette communauté et dans toutes celles où les taux de tuberculose sont très élevés.

Resumen

Carga de tuberculosis en Kampala, Uganda

Objetivo Determinar la prevalencia y la incidencia de tuberculosis en una de las áreas periurbanas pobres de Uganda.

Métodos Se realizó un muestreo polietápico para seleccionar una muestra de hogares a cuyos miembros se evaluó para determinar la presencia de signos y/o síntomas de tuberculosis activa; los antecedentes de tratamiento antituberculoso, y las características demográficas, socioeconómicas y del entorno doméstico pertinentes. Los pacientes con presunta tuberculosis fueron sometidos a una evaluación estandarizada para determinar si padecían la forma activa de la enfermedad.

Resultados Se evaluó una muestra de 263 hogares con un total de 1 142 personas. Se determinó que 19 de ellas habían tenido tuberculosis durante el periodo de referencia de un año (mayo de 2001 - abril de 2002): nueve casos (47%) ya habían sido

diagnosticados a través del sistema de atención de salud, y 10 casos (53%) se diagnosticaron en el curso de la encuesta. La prevalencia de todas las formas de tuberculosis y de los casos con esputo positivo fue de 14,0 (intervalo de confianza (IC) del 95% = 7,8-20,3) y 4,4 (IC95% = 0,83-7,89) por mil, respectivamente. La incidencia de todas las formas de tuberculosis y de los casos con esputo positivo fue de 9,2 (IC95% = 3,97-14,4) y 3,7 (IC95% = 0,39-6,95) por mil al año, respectivamente.

Conclusión La tasa de tuberculosis en esta comunidad periurbana era excepcionalmente alta, y posiblemente los actuales sistemas de vigilancia subestiman esa cifra. Urge implementar intervenciones encaminadas a reducir la transmisión de tuberculosis en estas y otras comunidades similares con altas tasas de casos.

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