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Dracunculus medinensis (Guinea Worm Disease) Elimination and Eradication and the Challenges of Emerging Non-human Animal Hosts: A Review of the Literature

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Systematic Review

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ABSTRACT

The objective of the review is to update information on the recent state of the transmission of dracunculiasis. Dracunculiasis is an ancient debilitating disease that has been lingering among dwellers of rural communities in some neglected sub-tropical and tropical countries. The disease is transmitted through drinking water that has been infested with Cyclops, the intermediate host of *D. medinensis*. Guinea worm disease has neither medicine for cure nor vaccine for prevention but can be prevented using certain intervention strategies. Any person that lives in the affected localities and drinks from Cyclop-infested water bodies could be infected, irrespective of age, gender or social status. The disease cripples the economy of affected communities, as it reduces attendance to farm work and other occupations and renders students absent from schools, through incapacitation. Eradication of dracunculiasis has been targeted using health education, boiling of water before drinking, application of temephos (Abate) to drinking water sources, filtration of water before drinking and installation of boreholes for the endemic localities. Attempts for eradication of dracunculiasis had reached an impressive and significant level before the emergence of cases of non-human animal infections. This phenomenon has sustained transmission of the disease in a few African countries. Published articles in Pubmed, Medline, Google Scholar and DOAJ on Guinea worm

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elimination and eradication and those on animal infections with Guinea worm were reviewed using Google search engine between February and April 2020. Scale up of application of Abate to affected drinking water sources is recommended as the most reliable and sustainable intervention in highly neglected communities.

Keywords: Animal hosts; dracunculiasis; elimination; eradication; literature.

1. INTRODUCTION

Guinea worm disease, otherwise known as dracunculiasis is a preventable, non-fatal but debilitating disease of neglected poor rural dwellers, who have no access to potable water. The disease is among the neglected tropical diseases, a group of diseases that is prevalent in many tropical and sub-tropical developing countries that are poverty -stricken [1]. Dracunculiasis is summarized as a disease of poverty and cause of poverty. The afflicted localities are either by omission or commission, neglected by their governments and the disease impacts more negatively on the people by interfering with their economic and educational development. The disease has been described as an affliction of poverty which debilitates people who dwell in remote and marginalized communities in sub-Sahara Africa [2] and some other developing tropical and sub-tropical countries of the world.

Dracunculiasis is an ancient disease that is almost as old as mankind and has documented far-reaching historical records of existence with mankind. The disease has been described as an affliction of mankind since antiquity and was referred to as the "fiery serpents" among the Israelites [3], as documented in the Christian Holy Scriptures. Barry [4] described it as a disease of antiquity with its archaeological remains reportedly recovered in Egyptian mummies and also concurred with its reference in the Old Testament of the Christian Holy Scripture as the "fiery serpent" that tormented the Israelites in the desert. Guinea worm disease has been described as a very painful and debilitating water-associated neglected tropical communicable disease with multiple adverse consequences on the health, agriculture, school attendance and overall quality of life of the affected communities [5]. The disease is caused by a parasitic nematode known as Dracunculus medinensis. Infection with D. medinensis occurs by drinking from stagnant water bodies such as ponds, cisterns, pools, drying river beds and shallow unprotected wells that have been contaminated with cyclops which are infected

with Guinea worm larvae. Cyclops are a group of crustaceans that has many species that serve as intermediate hosts of *D. medinensis.*

2. METHODS

Published articles on Guinea worm disease, especially those that relate to elimination, eradication and involvement of non-human animal infections were searched for and reviewed. Google search engine was employed to access published articles by big research organizations like the WHO, CDC and some other authorities in the area. Articles published by abstracting and indexing bodies including Pubmed, Medline, Google Scholar and DOAJ were consulted on the course of the review. Tables and figures were modified from their original sources and such sources were dully acknowledged by referencing them.

2.1 Life Cycle of *D. medinensis*

The life cycle of D. medinensis begins when a human being drinks untreated water that contains copepods (cyclops) that harbour the infective third stage (L₃) larvae of Guinea worm. Inside the stomach of the person, the actions of the gastric juices kill the cyclops and release the L₃ larvae, which thereafter, penetrate the host's stomach and the intestinal wall and find their way into the abdominal cavity and retroperitoneal space. The male and female worms copulate and the fertilized females migrate to the subcutaneous tissues, with predilection for lower extremities. The male worms eventually die after mating. Approximately a year post-infection, the gravid female worms induce painful blisters that eventually rupture and allow the worms to begin to emerge from the skin of the host, especially when it has contact with cold water. As the open blister comes in contact with cold water, the emerging Guinea worm discharges the larvae into the water source.

If within 3 days, the immature larvae find a cyclop intermediate host, they are ingested by the cyclop, otherwise, they die. The ingested larvae in the cyclop molt twice after 2 weeks and finally develop into the infective L_3 larvae. Ingestion of any L_3 larvae - infected cyclop by humans, completes the life cycle of the parasite.

2.2 Epidemiology, Health and Economic Consequences of Dracunculiasis

An infection with Guinea worm has an incubation period of approximately 12 months. People in endemic communities in the tropical countries become infected during the dry season when running streams have dried up, leaving only stagnant water bodies as the only sources of drinking water. Such bodies of freshwater like the ponds, pools, cisterns and unprotected wells are very conducive aquatic environments for the cyclop intermediate hosts to thrive. Age and occupation are important determinants of infection with D. medinensis. Dracunculiasis is known to occur in all age groups but is more prevalent among age group of 15-45 years old [5]. The type of work that people within this age bracket do could be a very important factor. Farmers, herdsmen, and water fetchers for domestic activities usually become more exposed and more infected than others [5]. Even in places with potable water sources, individuals in these occupations are usually infected more as their occupations take them away from homes where good water sources are available and are always tempted to drink from water bodies that are infested with cyclops while at work. The disease is not gender-specific because any exposed individual in endemic communities could be infected, irrespective of the gender.

Guinea worm disease has been reported to pose some debilitating effect on the patients as the worm emerges in the body, with manifestations of excruciating pain that is usually accompanied by fever, nausea and vomiting, swelling of feet, itching, and allergic reactions [6,7]. Secondary bacterial infections through open ulcers developed by the formed blisters, from which the worms emerge, may complicate the disease if the ulcers are not aseptically handled. Arthritis may set in and may be worsened as the disease progresses. Apart from the impact of many neglected tropical diseases, including Guinea worm on health of the people, they have been reported to be responsible for the people's social and economic burden and to maintain cycle of poverty by negatively affecting productive lives of the people and adversely affecting both sub-units and the whole of any endemic country [1]. The adverse effects of dracunculiasis on the health, school attendance, agriculture and the overall

quality of life of the affected people has also been documented by Morenikeji and Asiatu [8].

2.3 Concepts of Elimination and Eradication

Elimination and eradication are two terms in infectious diseases epidemiology that are related and seem to be same but actually different. Their relatedness makes researchers to use them interchangeably, even to the points of bringing confusion in their meanings. Fortunately, in the recent past, acceptable definitions that vividly explain the distinctions in the meanings have emerged. According to Dowdle [9], elimination is the reduction to zero of the incidence of disease or infection in a defined geographical area while eradication is permanent reduction to zero of the world-wide incidence of infection. Further explanations were made in order to make the definitions clearer. In elimination, there is always a need for sustained application of any introduced intervention measure so as to prevent re-establishment re-introduction and of transmission. This approach however, differs from eradication which is more advanced in that it emphasizes cessation of routine intervention measures as far as interruption of transmission has been certified. Based on these definitions, it becomes clear that elimination is more temporal and covers a limited geographical area while eradication is a permanent and global intervention [10]. In elimination, a relaxation or established complete cessation of the intervention measures encourages resurgence of the infection in question.

Eradication of any disease has always been the target of stakeholders in public health but not all diseases can be eradicated. Certain features of a disease determine whether its eradication is feasible or not. Richards et al. [11] and Aylward et al. [12] highlighted certain criteria that qualify a disease as an eradicable one and dracunculiasis possesses such criteria.

2.4 GWD Elimination and Eradication: Road Maps and Achievements

The campaign for eradication of dracunculiasis started in the 1980s. It has been documented that since 1986, the Carter Center has spearheaded the Guinea worm eradication effort in collaboration with other bodies including the WHO, UNICEF, Bill and Melinda Gates Foundation, other donor NGOs, Governments of endemic countries and numerous village volunteers [4]. The incidence of GWD has reportedly reduced from 3.5 million in 1986 [13] to 28 in 2018 [2,14], as depicted in Table 1. Many GWD endemic countries reportedly observed impressive percentage reductions in prevalence and incidence of dracunculiasis since the fight against the disease kicked off, with many of the intervention measures scaled-up in some endemic countries [9].

In 2019, the International GWD Eradication Campaign reportedly reduced annual human cases of dracunculiasis from 3.5 million in 21 countries to 49 cases in four countries – 43 in Chad, 4 in South Sudan, 1 in Angola and 1 in Cameroon [15]. Despite slight fluctuations in the wave of transmission in the current endemic countries, the Guinea Worm Eradication Programme that was launched with the ultimate aim of wrapping up the disease has made an impressive effort and progress in halting the transmission of the disease. Both number of endemic countries and the number of annual reported cases have significantly reduced, with only four countries - South Sudan, Chad, Ethiopia and Mali still having reported cases of GWD. The global cases were reportedly reduced from 3.5 million in 1986 to 77.863 in 1997 and the number of endemic villages, dropped from 22,000 in 1992 to 9,552 in 1997 [9]. Table 2 depicts progress made in eradicating GWD and the years of events across affected countries and continents.

 Table 1. Global number of cases of dracunculiasis in millions from 1986 to 2018 (modified from WHO [2])

Year of Observation	Cases in Millions		
1986	3.500000		
1990	0.623579		
1995	0.129852		
2000	0.075223		
2005	0.010674		
2010	0.001797		
2015	0.000022		
2018	0.000028		

Table 2. GWD eradication progress according to countries and continents (modified from WHO	
[2])	

Events	Country	Continent	Year
WHO certification as GWD-free	Pakistan	Asia	1996
WHO certification as GWD-free	India	Asia	2000
GWD transmission halted	Sudan	Africa	2002
GWD transmission halted	Yemen	Asia	2004
GWD transmission halted	Senegal	Africa	2004
GWD transmission halted	Cameroon	Africa	2007
GWD transmission halted	CAR	Africa	2007
GWD transmission halted	Mauritania	Africa	2009
GWD transmission halted	Benin	Africa	2009
GWD transmission halted	Uganda	Africa	2009
GWD transmission halted	Burkina Faso	Africa	2011
GWD transmission halted	Тодо	Africa	2011
GWD transmission halted	Niger	Africa	2013
GWD transmission halted	Nigeria	Africa	2013
GWD transmission halted	Cote d'Ivoire	Africa	2013
GWD transmission halted	Ghana	Africa	2015
GWD transmission halted	Kenya	Africa	2018
Current transmission as one or more infections	Mali [*]	Africa	Till date
	Chad*	Africa	Till date
	Southern Sudan	Africa	Till date
	Ethiopia*	Africa	Till date
	Angola	Africa	Till date

Key: GWD – Guinea worm disease. CAR – Central African Republic, *--Countries where animal infections occur

Different unrealized dracunculiasis eradication timelines have been set. GWD

Eradication was targeted by the WHO before 1990, in 1995, in 2005, in 2009 and in 2020. When certain unprecedented and uncontrolled epidemiological circumstances emerged, a new target year, 2030, a decade ahead, is expected. The repeated postponement in targeted years makes the eradication of GWD seem more of mirage than reality. Dracunculiasis has been reported to possess no medicine for cure, no vaccine for prevention and no known immunity can be developed against it [2]. It can only be controlled using combined intervention efforts that include preventing infected patients or animals from wading into a community source of water supply, boiling water before drinking, filtering of water before drinking, health education, surveillance and provision of portable water such as boreholes and tap water. It has been documented that if GWD is finally eradicated, it would be the first human parasitic infection to be wiped out and the first eradication to be achieved devoid of any vaccine or medicine [2,16].

Some important factors have immensely contributed to the sustenance of dracunculiasis in present endemic communities and encouraged the re-emergence of the disease in some areas where transmission has been halted and eradication probably taken place. Highlighted below are some of the factors.

- 1. Perception and attitude towards GWD: Despite sensitization, health education and enlightenment on dracunculiasis, people still regard the disease to be dependent on hereditary traits such as blood group type and genotype. Some even take it to be God's wrath on people who disobey Him, a belief that makes people to still drink from ponds and other cyclop- infested water bodies even if boreholes and taps are available. People also prefer the taste of water from such sources to water from taps and boreholes.
- 2. Presence of cyclop intermediate hosts of *D. medinensis* in sources of community water supply especially in areas with no boreholes and taps: This important phenomenon in the epidemiology of dracunculiasis can only be approached with the application of a cyclopicide known as temephos (Abate).

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- 3. Absence of maintenance culture and inadequate boreholes: Broken down boreholes are left unrepaired and when people do not have alternative access to portable water supply, they resort to the available sources such as the ponds, cisterns, pools and unprotected wells. In some communities where some boreholes are still functional, there are not sufficient to serve the teeming population. An observation of cases of inadequate or nonfunctional sources of safe drinking water has been made by Morenikeji and Asiatu [8] in their study in Oyo State, Nigeria.
- 4. Importation of cases of GWD: Political insecurity, wars and conflicts as observed in Sudan, can encourage importation of cases of GWD from current endemic areas to other areas or countries where the disease has never been reported before or has been eradicated. This condition is worrisome and requires effective and efficient surveillance systems.
- 5. Emergence of animal reservoir hosts: Domestic animal reservoir hosts of GWD such as dogs and cats, wild animal hosts such as baboons and aquatic hosts such as the fishes and amphibians have recently emerged. Their emergence has introduced significant doubt in the initially established optimism towards GWD eradication. Their appearance as hosts to D. medinensis species with identical molecular characteristics as those from humans, has introduced a strange life cycle, that differs from the conventional life cycle of the parasite and demands novel approach for intervention and eradication as has earlier been asserted by Cleveland et al. [17].

The influence of war and political instability that result in importation of cases and the emergence of non-human animal hosts of *D. medinensis* are principal drivers of dracunculiasis and cardinal foes against achievement of eradication of the disease.

(i) War and Political Instability: the Case of Sudan: It has been documented that the global campaign to eradicate GWD commenced at the United States Center for Disease Control and Prevention in 1980 while the conflict in Sudan resumed in 1983, after a-10year period of relief [18]. With resumption of the conflict, insufficient personnel, social, geographical and economic problems posed great challenges

to Guinea worm eradication in the country [3]. The influence of the ongoing war made Sudan to report more than half of the global cases of GWD annually [18]. As at the time of signing of Comprehensive Peace Agreement (CPA) in January 2005, South Sudan that seceded from Sudan, reportedly accounted for greater than 45% of the global cases of dracunculiasis [19]. The South Sudan Guinea Worm Eradication Programme that commenced in 2006 [19], employed multidisciplinary measures including comprehensive surveillance and efficient and effective communication networks to interrupt GWD transmission. Despite the full scale GWD eradication strategies implemented by South Sudan after the war, the disease still lingers probably because of the aftermath of the war and influence of other unidentified environmental factors, including the current strange non-human animal transmission.

(ii) Emerging Non-human Animal Hosts of D. medinensis: GWD transmission is currently prevalent in Chad, Ethiopia Mali and South Sudan [20]. It was expected that with the cessation of war and sustained impressive effort of the Guinea Worm Eradication Programmes (GWEPs) of different countries, the disease would have been eradicated. Unfortunately, the effort so far made by GWEPs of different countries in fighting the disease became challenged with great dismay. First, Chad that did not document any case for a decade (2000-2010) reportedly started to record cases with a strange transmission pattern [21,22]. Chad Republic reportedly documented its last case of dracunculiasis in 2000 [23], an encouraging development in the GWD eradication effort that prompted a 3-year passive surveillance in the country which ended with no identified cases of GWD [24,25].

Unprecedentedly, 10 cases of the disease were reportedly confirmed in 2010 [21] and the scenario was followed by 10 more cases in 2011 [26]. Screenivasan et al. [27] described the resurgence of dracunculiasis in Chad after 10 years of interruption of transmission as an unusual epidemiological situation since the history of GWEPs and therefore asserted that the resurgence could have resulted from undetected imported cases. The peculiar nature of the epidemiology of dracunculiasis reported in Chad was that the cases were sporadic and dispersed instead of appearing in the usual pattern of clustering around contaminated water bodies and that dogs and cats were found infected with species of *D. medinensis* that were genetically determined to be *D. medinensis* species that infect humans [14]. The strange transmission pattern which was a big puzzle among parasitologists and epidemiologists, continued for 24 months before infected dogs with emerging *D. medinensis* that was identified to be indistinguishable from the species that infect humans were discovered [2,28].

Subsequently, aquatic animals such as amphibians and fishes were found to act as paratenic hosts and transport hosts respectively. Assumptions that dogs could become infected with *D. medinensis* either through ingestion of infected copepods when drinking water or via eating of infected amphibian paratenic hosts or fishes transport hosts was raised [15].The number of canine cases of GWD has been reportedly soaring from hundreds in the early 2010, to more than a thousand five hundred (1500) in 2019 [14].

However, less number of infected cases than reported in Chad Republic has been known to occur in dogs in Ethiopia and Mali and Baboons have also been infected in Ethiopia. Chad has been reported to have the highest number of animal dracunculiasis (N = 1, 901), from which the domestic dogs had the highest (N = 1,855) [29]. In 2019, a total of 1,927 dogs and 46 cats were reportedly infected in Chad and many other domestic and some wild animal cases were also reported in Ethiopia and Mali [2].

Because of the significant number of cases of dracunculiasis in dogs in Chad, the country has been noted to be the reservoir of GWD [33].

Eradication of Dracunculiasis: a Reality or Mirage?: Hope in eradication of GWD appears dashed as the future is seemingly bleak, following an unprecedented shift in the normal transmission pattern of the disease as a result of involvement of animal reservoir hosts in some countries. The emergence of some domestic and aquatic hosts of *D. medinensis* has complicated the life cycle of the parasite and thus questions the feasibility of eradicating the disease in 2030, the new targeted eradication year. Cairncross et al. [34] has earlier asserted that eradication of any human parasitic disease is always easy if there is no animal involvement as reservoir hosts of the parasite and that eradication attempts become more difficult if the reverse is the case. In the past, when GWD eradication was conceived, there was no documented evidence of animal involvement in the life cycle of *D. medinensis* and lack of such evidence is among the criteria that qualified GWD as an eradicable disease.

Another important aspect of the GWD that introduces hopelessness, confusion and bleak future in the eradication of dracunculiasis is the nature of its protective immunity. That an individual has suffered from GWD in the previous year does not prevent him or her from being infected in the following year. A more mysterious condition in protective immunity of the disease is the documented fact that some individuals in endemic foci appear infection-free despite being exposed to the infection [16] whereas others within the same locality are always infected on annual basis [35]. The cause of the disparity in immunity, whether genetic or otherwise is currently poorly understood and yet to be elucidated.

Two Key GWD Control Measures Relevant to Eradication: Provision of adequate potable water for the GWD endemic communities has always been the most reliable intervention in the control of the disease and is the hope to achieve eradication of dracunculiasis. It is unfortunate to state that corruption, poor maintenance, political instability and war that are the hallmarks of many developing countries have reduced the number of functioning boreholes and tap water sources to inadequate levels in some GWD endemic communities and to zero levels in others. Lack of insufficient sources of potable water in endemic foci has reduced the effort so far made in GWD eradication. People that live in such endemic foci have no options than to go back to ponds, pools, cisterns and other water sources that are infected with cyclops, as the only available sources of drinking water. The emergence of the non-human animal hosts of D. medinensis is another clog in the accelerated wheel of the eradication programme. Domesticated dogs and cats are always in free-range in most cases in the developing countries. These animals have free access to the unprotected village sources of water supply, sometimes with emerging Guinea worm. GWD endemicity is always sustained in communities by the presence of both cyclop intermediate hosts and the primate animals (definitive hosts). There is therefore the need to concentrate intervention efforts on controlling the domestic animal hosts and the cyclop intermediate hosts. However, eradication of dracunculiasis will be better achieved by emphasizing the combination of the following approaches, some of which have been earlier recommended by previous authors.

S/N	Country	Animal Taxa	Number of Infected Animals	Date of Reported Cases	References
1	Chad	Domestic dogs	1040	2018	CDC [30]
2	Ethiopia	Domestic dogs Cats Olive baboon	11 5 1	2018	CDC [30]
3	Mali	Dogs Cats	18 2	2018	CDC [31]
4	Mali	Dogs Cats	8 1	2019	CDC [31]
5	Ethiopia	Baboons Dogs	6 2	2019	CDC [31]
6	Chad	Dogs Cats	1927 46	2019	CDC [31]
7	Ethiopia	Dogs Baboons	13 1	2015	Beyene et al. [32]
8	Ethiopia	Dogs Baboons	12 2	2016	Beyene et al. [32]
9	Ethiopia	Dogs Baboons	3 1	2014	Beyene et al. [32]
10	Ethiopia	Dogs Baboons	3 1	2013	Beyene et al. [32]

 Table 3. Summary of animal infections in some countries

- (1) Establishment of D. medinensis surveillance task force that will be vested with the responsibility of ensuring that any infected dog or other wild animals (eg. baboons) suspected to be infected are caught and brought forward for proper examination and confirmation of infection. If any dog is confirmed infected with Guinea worm, such a dog will be tethered in order to prevent it from wading into the community's source of drinking water. The task force members will always be compensated by placing them on regular allowances paid by the GWEP of the affected countries. Molyneux and Sankara [22] highlighted the need for such surveillance in all countries previously certified as GWD free, so as to forestall occurrence of imported cases.
- (2) The entrails of both fish and other paratenic hosts such as the frogs (where frogs are eaten by people) should be buried beyond the reach of the dogs.
- (3) Zoo keepers in Guinea worm endemic areas should ensure that the primate animals do not escape so as to avoid invasion and wading into the communities' sources of water supply by such animals.
- (4) It is known that management of dracunculiasis involves immersing the affected part that has the emerging worm in cold water to enhance fast emergence and expulsion of the worm. Any water that may contain Cyclops and is used for this purpose should not be used in feeding any of the companion animals such as dogs or cats, because such an attitude could predispose them to Guinea worm infection.
- (5) Use of an organophosphate insecticide known as Abate (temephos) against the cvclop intermediate hosts of D. medinensis is among the conventional intervention strategies which has been effective and is still currently employed as a very successful intervention measure. The right dose of the cyclopicide and correct calculation of volume of water bodies have been noted to be important conditions that must be met in order to achieve efficacy [32]. Less emphasis has always been placed on treatment of community water supply sources such as the ponds and other stagnant water bodies that encourage the growth of cyclops. Rather, emphasis has always been on installation of boreholes and water taps. Provision of boreholes and taps in GWD endemic

localities are no doubts, the most effective and efficacious intervention measure against dracunculiasis. But the reality is that such potable water sources are either scarce or totally absent nowadays in many of the current endemic localities. This situation necessitates emphasis on treatment of the community natural water sources with Abate, as it is a more sustainable approach.

(6) The current trend in transmission of D. *medinensis* that involves non-human animals may have resulted from evolution of a new species of cyclops that could easily be swallowed and nurtured by dogs, cats and other primates, including the affected aquatic animals like the fish and the amphibians. Several known species of cyclops have been identified from the taxa of Mesocyclops, Metacyclops and Thermocyclops [36] and since the existence of those species, cases of nonhuman dracunculiasis were uncommon.

If ponds and other stagnant water sources that serve GWD endemic communities are properly and regularly treated with right doses of Abate (temephos) and dracunculiasis transmission is not interrupted, resistance of the cyclops to available organophosphate insecticide regimen should be suspected and when resistance becomes established, the need for research to introduce a more efficacious chemical may arise. Therefore, either mutation or resistance is the phenomenon that drives the unusual wave of transmission of dracunculiasis that involves nonhuman animals in some of the current endemic communities.

3. CONCLUSION

In conclusion, concentration of attention on treatment of water bodies with right dosages of Abate, a more cost effective and sustainable intervention, is recommended over any other intervention in order to achieve eradication of dracunculiasis in localities that are neglected by their governments.

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COMPETING INTERESTS

Author has declared that no competing interests exist.

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