THE
CARTER CENTER

Summary of the Twenty-Seventh Meeting of the International Task Force for Disease Eradication (ITFDE) October 17, 2017

The 27th meeting of the International Task Force for Disease Eradication (ITFDE) was convened at The Carter Center, Atlanta, GA, USA on October 17, 2017 to review the status of the global campaign to eradicate Guinea worm disease (dracunculiasis) and of research to understand and stop transmission of the parasite among dogs, particularly in Chad. The Task Force members at the time of this meeting were Dr. Stephen Blount, The Carter Center (Chair); Dr. Peter Figueroa, The University of the West Indies, Jamaica; Dr. Donald Hopkins, The Carter Center; Dr. Julie Jacobson, Bill & Melinda Gates Foundation; Dr. Hamid Jafari, Centers for Disease Control and Prevention (CDC); Professor David Molyneux, Liverpool School of Tropical Medicine; Dr. Patrick Osewe, The World Bank; Dr. Stefan Peterson, UNICEF; Dr. David Ross, The Task Force for Global Health; Dr. Dean Sienko, The Carter Center; Dr. Nilanthi de Silva, University of Kelaniya, Sri Lanka/WHO Strategic and Technical Advisory Group (STAG); Dr. Laurence Slutsker, PATH; Dr. Ricardo Thompson, National Institute of Health (Mozambique), and Dr. Dyann Wirth, Harvard School of Public Health. Six Task Force members (Blount, Hopkins, Jafari, Molyneux, Ross, Sienko) attended this meeting, and three were represented by an alternate (Mr. David Delienne for Peterson; Dr. Nana-Kwadwo Biritwum for Jacobson; Dr. Dieudonne Sankara for the World Health Organization [WHO]). Former U.S. President Jimmy Carter attended the entire meeting.

Presenters at the meeting, which was chaired by Dr. Stephen Blount, included Drs. James Cotton, Wellcome Trust Sanger Institute; Mark Eberhard, CDC; Vanessa Ezenwa, University of Georgia; Professor Robbie McDonald, University of Exeter; Drs. Sharon Roy, CDC; Ernesto Ruiz-Tiben, The Carter Center; Dieudonne Sankara, WHO; Julie Swann, Georgia Institute of Technology; Elizabeth Thiele, Vassar College; Michael Yabsley, University of Georgia, and James Zingeser, The Carter Center.

Global Overview and Status of Certification of Eradication

Thirteen laboratory-confirmed cases of Guinea worm disease were reported provisionally in January-September 2017: 12 cases in Chad and one case in Ethiopia, where a small outbreak was discovered at the end of September. Eight of the cases (62%) were contained in Chad. No cases had been reported in Mali for 22 consecutive months or in South Sudan for 10 consecutive months. Through the end of August, Chad had reported 708 infected domestic dogs and 11 domestic cats, Ethiopia reported 9 infected dogs and 4 baboons, and Mali reported 8 infected dogs and 1 cat.

For the first time since infected dogs were reported in Chad in 2012, the number of infected dogs so far in 2017 (708) is reduced compared to same period of the previous year (879) by 19% and

the number of Guinea worms emerging from infected dogs is reduced by 39%. This reduction is believed to reflect mainly the impact of tethering infected dogs until their worms have emerged, educating villagers to bury fish guts instead of discarding them on the ground where dogs can eat them, encouraging residents to always cook and cure aquatic animals well, and limited use of Abate. Seventy nine percent of dog infections in 2012-2016 occurred in March-August. Most infected dogs and humans in Chad reside in villages along the Chari River, where 1,862 villages are under active surveillance in 2017. The pattern of cases in humans since the current outbreak was discovered in 2010 remains unusual, with only 9-16 cases annually, located in different villages each year: of 94 villages with cases so far since 2010, only six villages had a case in a subsequent year, including three that had cases in successive years.

The outbreak in Ethiopia had affected at least six migrant male workers from Oromia Region who shared drinking water provided from a contaminated pond at their workplace on a commercial farm in an adjacent area of Gambella Region a year ago. Ethiopian authorities and staff of Ethiopia's national Dracunculiasis Eradication Program had begun to interview the patients, assess relevant water bodies for possible treatment with Abate, identify and monitor all seasonal workers on the implicated farm and other nearby commercial farms before January 2017 who may have drunk water from the contaminated pond, and establish active community-based surveillance in the affected areas.

The World Health Organization (WHO) has certified 198 countries, areas and territories as free of dracunculiasis transmission. Eight countries remain to be certified: four endemic countries (Chad, Ethiopia, Mali and South Sudan), two countries in the pre-certification stage (Kenya, Sudan) and two countries not known to have had indigenous disease since before the global campaign began (Angola, Democratic Republic of Congo). The governments of Angola and Democratic Republic of Congo are in various stages of preparing dossiers for consideration by the International Commission for the Certification of Dracunculiasis Eradication (ICCDE) and may be ready for review in 2018. Kenya and Sudan have submitted their Country Reports to WHO already. Kenya is tentatively scheduled to receive an International Certification Team (ICT) mission later in 2017 if the security situation following the presidential election permits; the ICT mission to Sudan has been postponed due to unresolved rumors of a few suspected cases. WHO continues to request quarterly reporting of surveillance activity in post-certified formerly endemic countries. By the end of September 2017 WHO had received reports of surveys among dogs in 21,952 households in 1,947 villages in eight formerly endemic countries; these surveys found no dogs or humans infected with Guinea worm disease.

Biology and Life Cycle

Studies to date have revealed findings that suggest transmission of Guinea worm parasites in Chad involves a paratenic or transport host and that frogs may be more susceptible hosts than fish, but other aquatic animals such as Nile monitor lizards (*Varanus niloticus*) may be involved also. *D. medinensis* has been recovered from a wild caught frog in Chad and catfish (*Synodontis*) native to Chad have been infected experimentally. Third stage larvae of *Dracunculus insignis*, which is indigenous to North America, have remained viable in frog tissues for up to eight months in the laboratory. Dogs can drink copepods in high concentration from bowls of water under

experimental conditions, but more studies are needed to determine how many copepods they may ingest during a typical drinking event at copepod densities observed in the field. Copepods found in Chad are not unique from species found in other African countries where Guinea worm disease was endemic.

It is not clear why frequent infection of dogs with Guinea worms appeared in Chad when it did. Elders and leaders of the earlier Guinea Worm Eradication Program in Chad confirm that infections of dogs were not seen before the current outbreak. Recent ecological changes in the Lake Chad basin associated with over fishing and drought may have played a role. As fish stocks declined fishermen use smaller nets and people are eating and discarding smaller fish (2-3 inches long), which are the ones most frequently using copepods as food. The small fish usually are not cleaned before eating and they are often eaten uncooked. Agricultural use of pesticides on farms near the Chari River has reportedly declined in recent years and may have caused copepod populations to increase. Seasonal mass fishing has been practiced at the end of the dry season for generations along the river; it is not new. People garden in the river bed during the dry season and move inland to farm during the rainy season. Evolutionary changes in Guinea worm parasites themselves are not a likely explanation for the rapid changes observed in Chad, as these would only occur over a much longer term.

Preliminary results of an epidemiologic investigation conducted in July-August 2017 to determine risk factors for sporadic Guinea worm infections in humans, including risk factors potentially shared with dogs, and to pilot test a questionnaire for a future case-control study of infected dogs, suggest that drinking water from uncovered hand dug wells appears to be associated with Guinea worm disease in humans, but found no difference between cases and uninfected controls who used other unprotected sources of drinking water. This initial study found no evidence to confirm consumption of aquatic animals by humans or support presence of infected dogs in the village as risk factors for Guinea worm disease in humans.

Molecular/Genetic Studies

There is no evidence of genetic differences between Guinea worms from infected dogs and those from human victims in Chad. The worms are indistinguishable and appear to be the same species, *Dracunculus medinensis*. The Guinea worms in Chad, however, are unusual epidemiologically compared to worms in other countries by infecting dogs much more frequently and not causing outbreaks or cases among humans in successive years in the same village. The genetic diversity of Guinea worms in Chad is high and they are generally distinct from worms in other endemic countries. The genetic findings suggest that Guinea worm parasites were circulating in Chad during the period from 2001 to 2009 when no cases were reported. Surveillance for the disease was poor then and it was also a period of much civil unrest and political strife in Chad. Molecular studies also reveal genetically restricted populations of Guinea worms remaining in Mali and South Sudan, which suggests that those two countries are closer to stopping transmission than Chad and Ethiopia, where the populations of Guinea worms are more diverse genetically.

Dog Ecology and Diet

Use of GPS collars and examination of stable isotopes in dog whiskers are feasible ways to track dog movements and study dietary preferences of dogs in Chad. Dogs in Chad range over a small area closely associated with their owners. They rarely visit the river but frequent a few small ponds often in the middle of the village close to their residence. Preliminary findings are that providing clean drinking water appears to be protective somehow against dog infections with Guinea worms, while increased consumption of fish is a risk factor for dog infection. Dogs are sentinels for Guinea worm contamination in the environment.

Anthelminthic Treatment of Dogs

Investigations to date have shown that mass prophylactic treatment of dogs in rural Chad with Advocate/Advantage® (Bayer) or Heartgard® (Merial) is feasible. Over 5,000 dogs in 88 villages have been treated monthly with Advocate/Advantage administered topically since October 2016 and over 200 dogs have been treated monthly with Heartgard administered orally since September 2016. Both treatments are well accepted by the dogs and their owners. No impact of Heartgard on Guinea worm infection is evident to date; results of the Advocate/Advantage trial should be available early in 2018. Researchers also plan to examine the effect of Advocate/Advantage treatment on Guinea worm larvae from adult worms in experimentally infected dogs and ferrets.

Mathematical Modeling

Researchers have constructed models to explore different parameters and assumptions about the life cycle and ecology of Guinea worm transmission in people and animals, such as via a paratenic host or by drinking water, lifetime of the paratenic host, duration of larval viability in the host, and timing of the rainy season, and to compare the ability of different interventions to prevent or reduce the intensity of infection. Initial results simulating dogs' ingestion of water or infected lizards both appear to match actual data from Chad, and suggest that tethering infected dogs is effective in reducing infection, but Abate treatment does not interrupt transmission under current assumptions. Future work will extend and refine the model to include infections of humans and test the effectiveness of different interventions singly and in combination and at different levels of coverage. Other work will seek to identify factors associated with the presence and clusters of infected dogs in villages.

Conclusions and Recommendations

1. The ITFDE commends the continued progress of the global Guinea Worm Eradication Program since the previous review two and a half years ago, with cases in humans reported only from Chad and Ethiopia so far in 2017, 22 months and 10 months since the most recent indigenous cases in Mali and South Sudan respectively, and a 19% reduction in the number of infected dogs in Chad. The unfortunate recent outbreak of a few cases in Ethiopia requires special attention but so far appears manageable.

2. The ITFDE commends the robust research agenda being pursued related to dog infections in Chad, and endorses the on-going search for relevant intervention tools, including modeling of transmission scenarios and study of dog diets and habits.
3. Research priorities also should include continued attention to the mode of transmission, especially (dog) lapping studies and duration of larval viability in aquatic animals. At this stage, it is not possible to rule out transmission of Guinea worm infections in Chad via drinking water or eating a paratenic host, or both modes of transmission. Frogs appear to be a more likely paratenic host than fish so far.
4. It would be instructive to look for any differences between behavior of dogs and humans in households with and without Guinea worm-infected dogs.
5. Genetic studies indicate that the Guinea worms recovered from animals and people in Chad, Ethiopia and Mali are all *Dracunculus medinensis.*
6. The relatively small genetic diversity of Guinea worm specimens from Mali and South Sudan suggests that those two countries are closer to elimination of transmission than Chad and Ethiopia. Genetic findings also suggest that Guinea worm parasites were circulating in Chad during the decade when no cases of the disease were reported there.
7. In Chad, intervention priorities should stress active surveillance, intensified use of Abate wherever possible, increased containment rates for infected humans and animals, thorough cooking or curing of aquatic animals, burial of fish guts, and focus on Chadian villages with the highest number of infected dogs. The GWEP and government of Chad are urged also to advocate with utmost urgency for provision of safe sources of drinking water to all villages with infected humans or animals lacking a safe source of drinking water.
8. Prompt reporting and containment of Guinea worm infections in humans and animals are both important, since the worms from both are indistinguishable. The ITFDE endorses the enhanced communication campaigns launched recently in Mali and Chad and soon to be launched in South Sudan and Ethiopia in order to increase knowledge of the cash reward and of prevention messages, and help prepare countries for certification of eradication.
9. The ITFDE emphasizes the need for strong political support in all of the endemic countries remaining, which has been particularly forthcoming in South Sudan and to a degree in Mali. This need is now still especially acute in Ethiopia, as was specifically noted in a recommendation at the ITFDE meeting in 2015, and also in Chad.
10. The Task Force encourages engagement of regional health authorities in Oromia and Gambella in response to the recent outbreak in Ethiopia, including activation of the Health Development Army and Health Extension Workers in those two regions especially.
11. Insecurity is a significant hindrance to surveillance and interventions, and to validation of interruption of transmission as well as certification of the elimination of transmission of *D. medinensis* in Mali and South Sudan especially, but to a lesser extent in Ethiopia and Chad as well.