

► In 2010, the genomics institute BGI in Shenzhen was estimated to host more sequencing capacity than the entire United States. This was thanks to its equipment, purchased from Illumina of San Diego, California, which at the time represented state-of-the-art technology. But Illumina has since sold upgraded machines to at least three other genomics firms — WuXi PharmaTech and Cloud Health, both in Shanghai, and the Beijing-based firm Novogene.

Jason Gang Jin, co-founder and chief executive of Cloud Health, says that this trio, rather than BGI, will be the main sequencing support for China's precision-medicine initiative — although BGI's director of research, Xu Xun, disagrees. Xu says that precision medicine is a priority for BGI and that the organization has a diverse portfolio of sequencers that still gives it an edge. "If you are talking about real data output, BGI is still leading in China, maybe even globally," he says. BGI has already established a collaboration with the Zhongshan Hospital's Center for Clinical Precision Medicine in Shanghai, which opened in May 2015 with a budget of 100 million yuan and is run by Fudan University.

NUMBERS GAME

Regardless of the details, Jin thinks that China will be faster than the United States at sequencing genomes and identifying mutations that are relevant to personalized medicine because China's larger populations of patients for each disease will make it easier to find sufficient numbers to study.

Still, it remains to be seen whether China has the resources to apply these insights to the individualized care of patients. "China wants to do it, and everybody is very excited," says Ta Jen Liu, project director at the MD Anderson Cancer Center in Houston, Texas, who helps to establish collaborations in China and is familiar with the precision-medicine scene there.

But there are hurdles. He notes that Chinese researchers and pharmaceutical companies have not had much success in developing drugs so far; that the pathologists needed to diagnose specific diseases are scarce in China; and that physicians there are notoriously overworked. "Doctors are always overwhelmed with patients, seeing 60 or 70 a day," he says. "They don't have time to sit down and think about what is best for specific patients."

David Weitz, a physicist at Harvard University who is starting a company in Beijing to develop diagnostic instruments for use in precision medicine, agrees that there will be obstacles, but notes the initiative's assets. "We need lots of data to validate ideas, to validate tests," he says. "There's lots of data here."

He thinks that this, combined with the Chinese government's determination to succeed, will mean that the effort will ultimately win out. "They really seem devoted to meeting the needs of the society," he says. "It's an exciting thing, to try to help that many people." ■



Most cases of Guinea-worm disease in Chad have occurred in communities based along the Chari River.

INFECTIOUS DISEASE

Dogs thwart end to Guinea worm

Epidemic in dogs complicates push to wipe out parasite.

BY EWEN CALLAWAY

A decades-long push to make Guinea-worm disease the first parasitic infection to be wiped out is close to victory. But a mysterious epidemic of the parasite in dogs threatens to foil the eradication effort.

"If we're going to be aggressive and achieve this, we have to eliminate the infection in dogs," says David Molyneaux, a parasitologist at the Liverpool School of Tropical Medicine, UK.

The Carter Center in Atlanta, Georgia, is leading the global campaign to eradicate Guinea worm. Next week, it will announce that case numbers for the excruciatingly painful infection are at a record low, with approximately 25 cases reported in 2015 in just 4 countries: Chad, Ethiopia, Mali and South Sudan. But infections in dogs are soaring in Chad, where officials will meet at the end of January to grapple with the canine epidemic. The central African nation recorded more than 450 cases of Guinea worm in domestic dogs last year — an all-time high (see 'Canine comeback').

Researchers and officials strongly suspect that dogs are spreading the infection to humans; now the race is on to understand how this might happen, as well as how dogs

acquire the infection in the first place. The World Health Organization is unlikely to declare Guinea worm eradicated until the parasite has stopped spreading in dogs, says Molyneaux, who is part of the commission that will make that decision.

In 1986, when the Carter Centre joined the Guinea-worm eradication campaign, there were an estimated 3.5 million infections annually, mostly due to poor sanitation and lack of access to clean water.

When people drink unfiltered water, they can swallow microscopic freshwater crustaceans called copepods, which Guinea-worm larvae infect. The copepods die, releasing the larvae, which mature and mate in the human intestine. Male worms die after mating, but adult females — approximately 80 centimetres in length — survive and slowly migrate out of the gut. About a year after infection, they burrow through their host's skin, usually around the legs and feet, sometimes taking weeks to fully escape. To cope with the searing pain, many people bathe in rivers and lakes, contaminating the water with the next generation of larvae. Although rarely fatal, Guinea worm can debilitate people for months and keep children out of school.

There is no vaccine against the parasite and no effective treatment, so eradication



PHILIPPE DESMAZES/AFP/GETTY

efforts have focused on providing clean water and changing people's behaviour, says Donald Hopkins, a special adviser at the Carter Center who is leading its Guinea-worm eradication efforts. People in areas in which the parasite was once rife have learnt to filter their water using cloths and to avoid re-contaminating water supplies. Even the most out-of-the-way villages now quickly contain cases and report them to health officials.

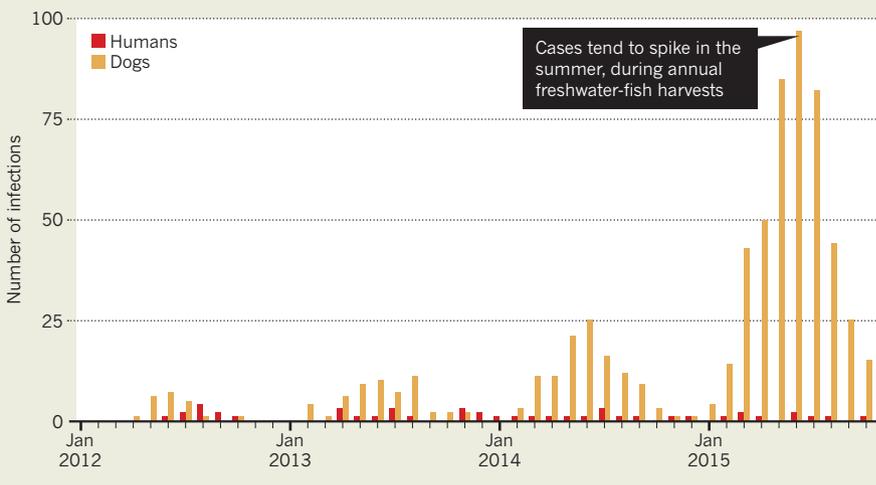
Chad was on the cusp of being declared free of Guinea worm in the late 2000s: no case had been recorded in the previous decade. But starting in April 2010, increased surveillance turned up a handful of human infections, and around 60 cases have been recorded since then.

The cases are unusually sporadic and isolated from one another, says Mark Eberhard, a parasitologist who consults on Guinea-worm eradication for the Carter Center. More typically, cases occur in clusters and recur in the same village year after year. "There was no increase or explosion of cases as one would expect," he says.

Shortly after these observations, officials began to hear rumours of Guinea-worm-infected dogs in Chad. Researchers have known for decades that dogs, leopards and other mammals occasionally acquire Guinea-worm-like infections, but they assumed that these cases stemmed from distinct species of *Dracunculus*, the nematode worm that causes the disease, or were rare examples of infections

CANINE COMEBACK

The number of Guinea-worm cases in dogs is soaring in Chad — a development that threatens global efforts to eradicate the parasite.



SOURCE: CARTER CENTER/GDC

that had somehow spilt over from an outbreak in humans.

But in Chad, researchers now think that dogs are spreading the worms to humans — not the other way around. Between January and October 2015, officials recorded 459 canine infections from 150 villages in the central African nation — an unprecedented volume. And genome sequencing has confirmed that dogs in Chad are infected by the same nematode worms (*Dracunculus medinensis*) that plague humans (M. L. Eberhard *et al.* *Am. J. Trop. Med. Hyg.* **90**, 61–70; 2014).

To better understand the situation, a team led by James Cotton and Caroline Durrant, genome scientists at the Wellcome Trust Sanger Institute in Hinxton, UK, is now sequencing the genomes of more Guinea worms collected from dogs and humans in Chad to confirm that dogs are indeed transmitting the disease to people. And Eberhard, who is convinced that this is the case, is trying to determine how dogs become infected in the first place. They are unlikely to contract the worms from drinking water, he says, because dogs tend to scare away copepods when they lap. Most of Chad's cases have occurred among fishing communities along the Chari River, and Eberhard

suspects that dogs are eating the entrails of gutted, copepod-eating fish. Dogs then pass the worms to humans by reintroducing the larvae into water.

Researchers, including Eberhard, are testing aspects of this hypothesis in ferrets, a common animal model in disease research, but eradication officials in Chad are not waiting for the results before taking action. Since February 2015, they have offered the equivalent of US\$20 to people who report Guinea-worm cases in dogs and tie up the animals to prevent them from contaminating water sources. They are also encouraging villagers to bury fish entrails to keep dogs from eating them. And a trial is ongoing to test whether a drug used to treat heartworm — a roundworm parasite common in dogs — has any effect on Guinea worm. Because of Guinea worm's one-year incubation time, it should be clear before the end of 2016 whether these interventions have worked.

Older residents from villages along the Chari River say that their fishing practices have not changed, according to Hopkins, and they cannot recall dogs becoming infected with Guinea worm in the past. But Molyneux says that the dearth of humans transmitting the disease could explain the parasite's jump to dogs. "If you were Guinea worm and there were only 100 of you left in the world," he says, "what would you do? You'd get the hell out of the host that's being targeted and move to something else." ■

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