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The disease that just won't go away

Around 3,000 people afflicted with kala-azar come in the way of India declaring itself free of the scourge, reports **Jacob Koshy** as he tracks down patients in West Bengal

Black fever: "India accounts for half the global burden of the disease, which is endemic to the subcontinent " Picture shows Rohim Sarkar during his check-up at a hospital in Malda. ▪ RITU RAJ KONWAR

At 17, Rohim Sarkar weighs as much as the average 11-year-old. When shirtless, each of the seven pairs of bones that make up his upper ribcage is visible from five feet away. An attending doctor at the Habibpur block hospital in Malda, West Bengal feels his spleen and the verdict is clear: "VL," he declares, followed by two other colleagues jotting the verdict and leading the boy aside for a confirmatory dipstick test, a detailed set of photographs, a skin biopsy and a recommendation that he "immediately" begin treatment.

Sarkar presented symptoms considered typical of visceral leishmaniasis (VL), or kala-azar, a disease that is endemic to a contiguous blob of districts spanning West Bengal, Bihar, Jharkhand and eastern Uttar Pradesh. Caused by the *Leishmania donovani* parasite, harboured by an insect called the sandfly, the Habibpur block, barely 30 km from Bangladesh, is considered particularly vulnerable to kala-azar outbreaks.

A parasitic disease

Kala-azar is a parasitic disease that is confined to humans, meaning that unlike, say, bird flu, there is no other animal that harbours the infection in Asia. Endemic to the Indian subcontinent in 119 districts in four countries (Bangladesh, Bhutan, India and Nepal), India itself accounts for half the global burden of the disease. If untreated, kala-azar can kill within two years of the onset of the ailment, though the availability of a range of drugs for almost a century has meant that less than 1 in 1,000 now succumb to the disease. According to numbers from the Union Health Ministry, 2016 was the first year that no kala-azar death was reported in India. Experts, however, note that like malaria and several other vector-borne diseases in India, the government only considers lab-confirmed and officially registered deaths and therefore, frequently underestimates both caseload and mortality.

Historically, a 20-day treatment schedule with sodium stibogluconate (SSb) injection and the spraying of the malarial insecticide dichlorodiphenyltrichloroethan (DDT) in houses and surroundings were the only weapons against the disease.

When DDT was used as part of the malaria eradication programme, very few cases of kala-azar were reported. When the use of DDT was stopped a few years later, there was an increase in the number of kala-azar cases.

Over a period of time, resistance to the only drug (SSb injection) led to frequent outbreaks and fatalities and the Union Health Ministry, which had committed to eliminating kala-azar by 2010, revised it to 2015. Bangladesh, India and Nepal committed to eliminate the disease from the region, where elimination (as opposed to eradication) is defined as no more than one case per 10,000 population at the upazila level in Bangladesh, sub-district (block PHC) level in India and district level in Bhutan and Nepal.

Since 2003, India's National Vector Borne Disease Control Programme (NVBDCP) is in charge of coordinating with endemic States to eliminate the disease. With funds from a World Bank-supported project (2008-2013), the NVBDCP now funds consultants at State and district level and Kala-azar Technical Supervisors (KTS) at the State's blocks (or clusters of village panchayats) to conduct active surveillance. That means local village health workers (Accredited Social Health Activists or ASHAs) are entrusted with constantly visiting houses and looking for patients who may present symptoms of the disease and alert health authorities.

Several new medical advances have aided the fight against kala-azar. A rapid diagnostic test, called rK39 can – with a pinprick of blood – indicate the presence of the parasite. With SSb injection on the decline, there are now two mainline drugs, miltefosine – originally conceived as an anti-cancer drug and taken orally – and liposomal amphotericin B (LAmB), a drug that once needed to be injected at regular intervals over four weeks but now only requires a single shot. These, besides an array of genetic tests that have obviated the need for painful jabs to the spleen and liver to confirm the presence of parasites, and global and national political commitment in terms of funding research and drug dispensation, has meant that kala-azar may be on the verge of being stamped out. However the 2015 elimination target was missed and postponed to September 2017, again a deadline that won't be met. This, in spite of the number of kala-azar patients plummeting from 36,000 in 2005 to 2,969 in 2017, according to Central government figures.

At the camp

Sarkar is one of 57 residents who've made it to the Habibpur hospital as part of biannual medical camps organised as part of the active surveillance process. About 160 were expected but a bus strike has thwarted attendance. West Bengal, like the other endemic States, was to have eliminated kala-azar in 2015, but is set to miss the deadline this year too despite the number of patients in the State coming down from 2,700 in 2005 to less than 50 as of this July.

Among the camp attendees, seated on the rows of wooden benches that made up the capacious common hall of the hospital, Sarkar was the only one who presented the typical symptoms – the emaciation, anaemia and signs of a puffed spleen – that have helped doctors quickly ferret out kala-azar cases for almost a century. More than Sarkar, however, what worried the visiting doctors were 20 outwardly healthy occupants of those benches. Most were once kala-azar patients and, as the doctors who screened them found, are stricken in various degrees by a mixture of blotches and ulcers on their hands, legs, backs and, sometimes, on their faces.

Painless and never known to trigger the fevers and pains typical of parasitical diseases, the blemished skin is the only sign of post-kala-azar dermal leishmaniasis (PKDL). It isn't the kind of disease that prompts villagers of Habibpur block, who besides kala-azar also live under the constant threat of malaria and tuberculosis, to skip farm work or forego a day's earnings from manual labour, to line up outside hospitals. "One of the patients with PKDL told me that the only reason he wanted treatment was because he was looking to get married," says Dr. Mitali Chatterjee, a medical doctor and researcher at the Institute of Post-Graduate Medical Education and Research (IPGME&R), Seth Sukhlal Karnani Memorial Hospital, Kolkata, which is known informally as the "PG" hospital.

PKDL results from the parasites left over from a kala-azar infection that couldn't be slain by the chemical cocktails used to treat kala-azar. Though harmless, the pigmented skin can provide harbour, says Chatterjee, to the parasites and they can make their way onto other sandflies. Like the anopheles mosquito, the sandfly needs human blood to nourish their larvae and in the process can pass on parasites to new people and trigger a kala-azar infection. Roughly a tenth of those with a history of kala-azar will go on to develop PKDL and, potentially, seed a fresh outbreak. The precise reason for this isn't known yet. "In the 1970s or early '80s, VL [kala-azar] had almost disappeared and then there was suddenly an epidemic," says Srija Moulik, a research scholar at IPGME&R, "it was later traced back to a single case of PKDL. There's a paper on that."

Case and cure files

The earliest empirical evidence for a link between PKDL as a silent agent provocateur for kala-azar outbreaks and DDT sprays came in the 1990s from C.P. Thakur, a physician and now a BJP Rajya Sabha MP. He reported an unusual trend in kala-azar cases in Bihar. Between 1970 and 1989, 530 individuals were confirmed with PKDL at the Patna Medical College (PMC), with the number of cases rocketing from two in 1970 to 59 in 1989. This was in contrast to no cases of this disease being reported at the PMC from 1958-1970. In the period 1977-1990, there were 3,01,076 cases of kala-azar reported in Bihar alone, with a mortality rate of over 2% (compared with 31,074 cases and a mortality rate below 0.4% for the rest of India). "It seems possible, that once DDT spraying stopped, the re-establishment of large sandfly populations and infection of these vectors, largely as a result of them feeding on cases of PKDL, provoked the resurgence of kala-azar," Thakur and co-author K. Kumar reported in the June 1992 edition of the *Annals of Tropical Medicine and Parasitology*.

Even though this link between kala-azar and PKDL was hinted at since 1922, it wasn't until 2005 that the World Health Organization (WHO) and health authorities in India, Nepal, Bangladesh, Sudan (who together account for 90% of kala-azar cases) began concerted efforts to eliminate PKDL, as part of kala-azar elimination strategies.

In a round-up of the country's progress in dealing with the disease, at a conference in Bengaluru earlier this year, Chatterjee showed a slide illustrating that in spite of the rapid dive in kala-azar cases across endemic States, PKDL cases in Bihar, which bears 70% of India's kala-azar burden, had risen to 500 from nil in 2013; from 300 in 2013 to 900 in 2017 in Jharkhand and 50 to 250 in West Bengal, in the same period. To Chatterjee, however, the rise in cases indicates States' increased efforts to find kala-azar patients and hidden PKDL cases becoming manifest.

At the IPGME&R, one of the nodal research medical labs in Kolkata that's part of the kala-azar surveillance-detection-and-analysis network, scientists are finding out through DNA analysis that the leishmaniasis parasite is an extremely resilient entity and can be dormant in the body and seed infections even after as many as five years.

The group of mostly-women scientists, who are trying to cleave apart the mysteries of the parasite, are located a five-minute walk away from a modest building that once hosted the laboratory of Sir Ronald Ross, the India-born British Nobel Laureate who established that mosquitoes were responsible for transmitting malaria. Ross was also the one who christened the kala-azar parasite as *Leishmania donovani*, after the scientist duo that discovered them.

Over the days spent peering through blood samples and skin biopsies from medical camps such as at Malda, Moulik points to yet another possible chink in the government's artillery to weed out kala-azar. The single injection of LAmB, which is now used to treat kala-azar, dramatically reduces the number of parasites in the blood and can cure the infection. However, when PKDL patients were subjected to the same medicine (targeting the same parasite), it didn't completely clear the parasite load. On the other hand, prior to LAmB, the treatment of choice for kala-azar was miltefosin, which is an oral pill taken over 12 weeks. It usually brought about nausea and other discomfort because of which several patients would quit treatment midway. However Moulik points to data in the lab that shows miltefosin did a superior job in flushing out the parasites from PKDL patients. There is a catch though. The ultra-sensitive probes that Moulik employs can spot parasites only if there are at least 10 of them in a microgram of DNA. It is quite possible that a patient might be well and disease-free for a few years but have a miniscule amount of parasites that will multiply at an opportune time in, say, five years, and then radiate the vicious cycle of outbreaks and epidemics that has undermined anti-kala-azar programmes through the years. "I believe that if parasite loads go down to 10, the body's immune system should ideally stave off infection but this is indeed the million-dollar question: 'How long till we are sure that the parasite loads never increase enough to pose a threat?'" says Moulik.

Patients waiting for their examination at a medical camp in Malda.

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> DR. MITALI CHATTERJEE,
> Doctor and researcher, Kolkata

The ground realities

The Habibpur hospital, from where IPGME&R gets a significant number of patient samples, is as large as a single-screen movie hall with X-ray machines, photocopiers, beds and a handful of trained nurses. To get to it, one must cross a stream of stagnant water that, according to local residents, swells up during the monsoon. Within several areas of the hospital, debris is piled up. There is a mossy pool of garbage alongside a water cooler that is inaccessible to the most flexible of gymnasts.

The block medical officer is a busy man who must, alongside coordinating a kala-azar camp, dragoon the same set of field workers to fan out into the villages looking for tuberculosis, malaria and leprosy patients. Since 2015, when the government authorities woke up to the urgency of eliminating PKDL, patients are being given financial incentives. All those who complete the course of treatment will get ₹2,500 (and the medicines made available through the WHO network) and the village field staff, consisting of ASHAs and KTSs, stand to get ₹500 for every such patient. "If financial incentives are given, then we get patients," says a doctor who has been part of several field camps, "but almost never has a district medical officer accompanied us. They are supposed to."

English Mohanpur, an inexplicably-named village a few km away from the hospital, is a slushy hamlet between rice fields. Several tribal communities populate its interiors and Koel, an ASHA worker, says some of the tuberculosis and kala-azar patients also battle alcoholism. Few houses have concrete roofs and fewer still comply with the government directive to spray the houses with the insecticide synthetic pyrethroid, the replacement for DDT. These sprays are needed at regular intervals and need a thorough application in every room including the kitchen. "The problem is that the spray stinks and people say they'd rather risk kala-azar than bear with the smell," says Chatterjee. "There is also a cluster effect. Families stay very close together and one infected person can spread it to the others."

Sripad Mandal, 42, a daily-wage labourer and village resident, was bedridden for three months because of kala-azar. He says he visited the block hospital and was given a course of medicine but that didn't work. He wasn't given a second round of medicine at the hospital and finally had to get himself admitted to the Calcutta School of Tropical Medicine. He now claims to be well. His disease, however, manifested before the government announced financial incentives for completing the treatment. "This is the disease of the poorest of the poor. Unless socio-economic conditions are improved and better sanitation is available, I don't see just medicines and drugs completely eradicating kala-azar," says Chatterjee.

The English Mohanpur village, one of the worst-affected areas in Malda district.