In Search of Kala Azar: Bedbugs and Other Red Herrings

WHEN THE CENTURY turned to 1900 the epidemic in the Gangetic plain began to wane. After kala azar’s merciless half-century hold in Bengal, Bihar, and Assam, the demoralized and depopulated land slowly began to return to a more secure and prosperous life. Kala azar did not completely disappear; cases continued to occur, but at much lower, non-threatening numbers. However, when the epidemic ended, an inquiry could be pursued that was impossible when the disease first struck Jessore in 1824. Between 1824 and 1900 the concept of the causation of disease had undergone a radical change. It was as if medical science, during this brief period of time, had emerged from the long medieval night into the enlightenment. Louis Pasteur ushered in the new science with his studies on the microbial causation of “sick” beer and silkworms. By the 1870s he was extending his studies to the microbial pathogens of animals, and then to those of humans. It was not long thereafter that the Germans entered the game, led by the giant intellect of Robert Koch. Now microbial pathogens were being discovered almost monthly—cholera, plague, boils, diphtheria. It seemed then that microbes were everywhere; that all disease had a microbial etiology. There was an enormous excitement and vigor in the pursuit of the pathogen. The Zeitgeist of the period was expressed by old Dr. Gottlieb in Sinclair Lewis’s novel Arrowsmith, who “anoints” the young scientist with the benediction, “May Koch bless you!” Parasitic pathogens were also being discovered during those years; Laveran (as noted earlier) unearthed the malaria parasite in 1880, and J. E. Dutton found the trypanosome in a human sleeping sickness patient in 1902. Science and tropical medicine were being brought together. Paul Ehrlich’s work in Germany on dyes and drugs began the search and discovery of synthetically created, powerful chemotherapeutic agents. Diseases were beginning to yield up their secrets and they were yielding to cure by man-made drugs.

The diseases of the tropics were studied by scientist-physicians who were truly engagé. Some of the best minds that the ruling country had to offer went to the colonies. They watched birds, catalogued the fauna and flora, sat up nights in flimsy machans to kill tiger. They played polo, shot snipe—and pursued their microbial quarry with a tenacity that by today’s standards of paid-for-by-project research seems almost quixotic. So, when the old Queen went to her reward in 1900, there was already in place in India a medical research establishment staffed mainly by
military men of the Indian Medical Service. Other excellent research was carried out by medical men, such as tea estate physicians, working in remote areas under primitive conditions. It was at this time and in this climate that these men (and one woman) took off in hot pursuit to discover the causative agent of kala azar. It was a pursuit that would follow many false trails and scents before the *Leishmania* was bearded in its macrophage and sandfly dens.

It seems strange from today’s retrospect that the first false trail was laid down by a worm—the hookworm. The ancients were ignorant of the hookworm but aware of the disease it caused. Almost one thousand years ago a Chinese medical commentary epitomized it as the “able to eat but too lazy to work” disease. In 1838, a Milanese physician, Angelo Dubini, described the numerous small worms that he saw attached to the intestine of a dead Italian peasant whom he had autopsied. He saw the worms but didn’t understand what they could do. That was left to O. Wucherer, a physician born in Portugal of German descent and practicing in Brazil. In 1861 the Benedictine

7. There are two hookworms of humans, *Ancylostoma duodenale* and *Necator americanus*. The adult worms are attached by fanglike mouth-parts to the inner wall of the small intestine, where they assiduously suck the blood from small, ulcerous lesions at their attachment site. In time, with enough worms (and often compounded by other conditions such as iron-poor diet, malaria, and pregnancy), the constant loss of blood leads to a severe anemia—even death in the worst cases. Hookworms are both temperate and tropical in their geographical distribution. At one time they almost bled the American South white. The hookworms also caused great debility to miners because the then unsanitary conditions in mines and tunnels were highly favorable for hookworm transmission. Hookworm eggs pass out with the feces onto the soil and hatch into larvae which remain quiescent until trod on by the unshod human foot. They then penetrate the skin of the foot and make their way through the body to the intestine, where they grow to adult size, mate, and suck blood. In the tropics the barefoot boy is just as likely to be palely anemic as brown-cheeked.

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...monks of Bahia, with true Christian charity, called Dr. Wucherer to attend to a dying black slave they owned. The wretched man was at death’s door, so severely anemic that his blood was almost water. The next day the slave died, and over the strong objections of the monks, Wucherer did a postmortem examination and found masses of “Dubini’s worms” clamped to the intestinal wall. From this he made the association between the parasite and the “hypoaemia.” Thus, in 1890, when a commission was sent to Assam to investigate the cause of kala azar, they searched for the then known agents that could cause severe anemia, and they thought of hookworm. Hookworm was a natural prime suspect. And when the investigator in charge, Dr. Giles, examined the feces of inhabitants of kala azar-stricken villages, he did indeed find the characteristic thin-shelled eggs of the hookworm under his microscope. “Kala azar is hookworm,” said Dr. Giles.

“Not so,” said Surgeon-Major Dobson, also posted to Assam. Dobson’s choice was that malaria caused kala azar. It was conceded that hookworm would cause anemia, but in kala azar not only was there an anemia but there was also a big spleen, and splenic enlargement was not a consequence of hookworm disease. Malaria caused anemia and splenomegalic. Kala azar was malaria.

“Not so,” said Dr. Giles. The big spleen didn’t count. Practically everyone in Assam had had malaria. There were a lot of people without kala azar walking around with a big spleen. Besides, the fever of kala azar was not like that of malaria, it was more sustained and unremitting, and there was that progressive downhill slide to death that was atypical of malaria.

The malarialphiles (by 1896, Dobson was joined in his views by others) continued the forensic with the rebuttal
abdominal wall, and into the body of the spleen. Donovan expressed the plug of splenic tissue captured in the needle onto a glass slide, stained it, and examined it under the microscope. The organisms which Leishman had described were seen only in the splenic tissue of patients with symptoms typical of kala azar. By 1904 the organisms were recognized as being protozoan in nature. They were given the name “Leishman-Donovan bodies,” and later the taxonomic designation of *Leishmania donovani*.

But nomenclature is not an end in itself. The tidy housekeeping of biology demands that any newly discovered creature or plant be classified according to its affiliations—its family ties—siblings, near and distant cousins, the near and distant relatives of its extended family. In more exact terms, it would need a sorting placement within genus, family, class, and phylum. In 1903, *Leishmania donovani* was still a taxonomic orphan in search of its nearest relatives. Of more crucial importance, however, was the unsolved question of how *Leishmania donovani* got from A to B... from an infected person to its next host. The disease could not be effectively controlled unless the manner of its transmission was known. The spread of kala azar from household to household, and from village to nearby village, clearly indicated that it was an infectious disease. Was it carried in the air from the breath of the infected to the uninfected? Was it carried in the drinking water contami-

9. The discoveries made in India were the “main event” of the investigations on kala azar, and what happened, and is happening, in the Indian subcontinent is the theme of my story. However, as noted earlier, kala azar (visceral leishmaniasis) occurs elsewhere too and early research was carried out in those endemic regions. In 1903, Marchand described the parasites from a British soldier who died during the fighting near Peking. That same year Pianese found the organisms in smears from the spleen and liver of children dying of “splenic anemia” in southern Italy.

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nated by the excretions of the sick? By touch? By sex? By giving nursing care to the stricken? Or by another route that in 1903 was beginning to appear as a new possible mode of transmission—the blood-sucking insect?

In 1876, (Patrick Manson) who was to become the father of tropical medicine), working in Amoy, China, as a physician to the Chinese Imperial Customs Service, discovered that the filarial worm, the cause of elephantiasis, was transmitted by the mosquito. Then, in 1898, Ronald Ross in India and G. B. Grassi in Italy made the great discovery that malarial parasites were also transmitted by mosquitoes. So, by analogy, there were those who hypothesized a blood-sucking insect as the means by which *Leishmania donovani* got from A to B.

One of the first clues to both transmission and taxonomy came from the “test tube” cultivation of the parasite. It is all very routine today: you go to your doctor with your sore throat or other infected part, and a sample is taken for cultivation on artificial medium, the organism grown out, identified, and its sensitivity to various antibiotics determined so as to select the most efficacious one for your treatment. In 1903, when microbiology was in its lusty infancy, cultivation techniques were just being devised. It was essential to isolate, propagate, and identify the microbe in culture for research on the origin and treatment of infec-

10. It is said that Manson’s first encounter with elephantiasis was a Chinese peanut vendor whose serotum was so large that he used it as a counter to display his merchandise.

11. That a parasitic organism living in a warm-blooded host will undergo a profound morphological and physiological transformation to complete its cycle in the completely alien milieu of the invertebrate is a truly remarkable adaptation. We still have no real understanding of the cues and the consequent genetic activation that bring about these transformations.
tious diseases. In each case, the discovery of a new pathogen was quickly followed by an attempt to grow it under laboratory conditions. Sometimes it worked. Sometimes it didn’t. It was not, for example, until some seventy-five years after the discovery of the malaria parasite that the trick of getting it to grow in the “test tube” was worked out. For some microorganisms and parasites the culture trick has still not been elucidated.

Thus, when Leishmania donovani was identified as the cause of kala azar, the next natural step was to grow the organisms in man-made culture medium. In 1904, a year after Donovan’s confirmation of the causative organism of kala azar, Sir Leonard Rogers, working in Calcutta, put some spleen tissue from a patient into a simple salt solution nutriment “soup,” Sir Leonard must have been dumbstruck with surprise when, a week later, he peered down his microscope at a drop of the culture fluid. What he would have expected, if the culture was successful, was a multiplication of the Leishman-Donovan bodies, like so:

But that was not what Sir Leonard saw. The Leishman-Donovan bodies had transformed. From a minute ovoid form, they had become, in culture, spindle-shaped bodies some ten times the size of their midget Leishmanial parent, each bearing a single threadlike flagellum at the anterior end. These flagellated forms were multiplying by an asexual division in the culture fluid, like so:

This meant that the Leishman-Donovan bodies within the macrophages of kala azar patients were but one stage in the life cycle of the parasite. Culture had revealed that there was a flagellated stage also, and this made it a cousin of the trypanosome, relatives within the larger family of tissue and blood-dwelling flagellates collectively known as the hemoflagellates. Protozoologists had seen the same spindle-shaped flagellate organisms (we now call this stage/form the promastigote) elsewhere—within the intestinal tract of a variety of flies and bugs. It was therefore most likely that what happened in culture represented what would normally occur in the gut of a blood-sucking insect. Ergo! Transmission of Leishmania donovani from person to person was by the bite of an insect infected with these flagellate forms. A good and sound assumption; but culture provided no clue as to what the insect—or insects—might be. Another thirty years of intense research were to pass and many more false trails laid before the innocent flies of Dr. Chakravarty were proven to be the guilty party.
The bedbug, even when dignified by its Latin name of *Cimex lectularius*, is a loathsome creature. During the depth of night it creeps from its hiding places—whether the cracks of mud-walled havels in the tropics or the steam pipes and crannies of North America’s tenements—to feed on its sleeping blood supply. It’s not nice to have bedbugs. The scarred feeding marks on the bodies of poor children will attest to that. Logic would have it that any bug with as disgusting, blood-sucking habits as the bedbug must be a carrier of disease-causing microorganisms. And, God knows, there was no shortage of bedbugs in India. Thus, the bedbug became an early prime suspect as the vector of kala azar. Those who incriminated the bedbugs became highly partisan in their belief and there was, for some twenty-five years, the tantalizing but not quite conclusive experimental evidence that was to keep them steadfast to the bedbug red herring.

The chief champion of the bedbug-as-vector was Dr. W. S. Patton, who was conducting his researches in Madras. For five years, from 1907 to 1912, Patton fed bedbugs on kala azar patients. In the intestine of a few of the bedbugs that he dissected several days after their blood meal, he observed the flagellate “culture” form of the parasite. However, although the Leishman-Donovan bodies from the patients had transformed in the insect’s intestine, the flagellate-stage parasites could not be found in its salivary glands or mouthparts (by analogy, the infective form of the malaria parasite is in the mosquito’s salivary glands). Those glands would have to be the repository of the parasite if they were to be transmitted during the feeding process. Well, reasoned Patton, et al., if they don’t spit in you, they shit on you—transmission was by the infective route. The flagellate bodies were voided in the insect’s feces and made their way into the human body by abrasions on the skin or the small puncture made by the feeding bedbug.

Meanwhile, the bedbug was giving researchers a considerable amount of trouble. The flagellates tended to disappear from the bug’s gut after a few days and those organisms that did remain were mostly dead and dying forms. As for the feces, it was difficult to recover viable forms that would “return to life” in test tube culture medium. Not a candidate vector to bet one’s career on. Then, in 1922, the bedbug was dramatically rescued by a Mrs. Helen Adie. Mrs. Adie was a protozoologist working on kala azar in

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12. Over the years, the bedbug has been suspected, incriminated, and condemned as being the transmitter of a variety of parasites, bacteria, and viruses, but has always been proven innocent. As far as is now known, the bedbug’s bite does not transmit any infectious pathogens to humans. Lice were also an early suspect as the vector of *Leishmania donovani* but it was pointed out that the Bengali was clean of his person and rarely lousy. The bedbug, on the other hand, would bite the sleeping washed and the sleeping unwashed without partiality.

13. Salivary juice, “bug spit,” is essential to the blood-sucking insect. It contains powerful anticoagulants (which causes the itch and to which one can become allergically sensitized) that prevent the blood from clotting, and clogging in the small-bored “hypodermic-needle” mouthpart.

14. By analogy, this was not a totally unreasonable hypothesis. There is an allied disease present in the American tropics, Chagas’ disease, caused by *Trypanosoma cruzi*. It’s an un treatable infection that affects hundreds of thousands of people and may lead to death by heart failure or other cardiac abnormalities. It is transmitted by another blood-sucking bug, the Triatomid, which can slip its stiletto mouthpart into the sleeping person so artfully that its familiar names are the “kissing bug” and the “assassin bug.” The infective-stage forms of *Trypanosoma cruzi* are in the bug’s feces. When the Triatomid feeds, it takes in blood at one end and simultaneously defecates on the skin from the other end. The sleeping host may unconsciously scratch the bite and rub the parasites into the body through a lesion to effect transmission of the infection.
Calcutta\textsuperscript{15} who claimed to have actually found the \textit{Leishmania} in the bedbug's salivary glands. This would be almost positive proof that \textit{Cimex lectularius} was the One True Transmitter. It was summer and the government and health officials, anybody who was anybody, had moved to the hill stations. Mrs. Adie sent a telegram to the government sitting in Simla telling of her great news, and a few weeks later that telegram was published, \textit{in toto}, in the \textit{Indian Journal of Medical Research}. Adie's finding greatly buoyed Patton's cause. Later that year, he announced to the Indian Science Congress that the bedbug theory was now nearly complete.

In the meantime, Mrs. Adie's microscopical preparations of the infected bedbug salivary glands were sent to other experts and their judgment caused the rapid deflation of the bedbug-as-vector theory. The organisms in the glands were not \textit{Leishmania} but rather a completely unrelated protozoan parasite, \textit{Nosema}, that had a superficial morphological resemblance to it. \textit{Nosema} was known to be a common parasite of insects and even played a role in Pasteur's formulating the germ theory of disease from his finding the protozoan in sick silk worms. Even after all these years I can feel so sorry for Mrs. Adie . . . as would any other scientist who can appreciate the pain and embarrassment of having a great finding, a breakthrough, proved false because of a technical experimental error. I am happy to report that Mrs. Adie carried on. Two years later we find

\textsuperscript{15} Try as I might, I have been unable to trace the person of Mrs. Adie. She was a medical protozoologist, as were several other distinguished women scientists in the era between the two world wars (and also today). She had, however, the singular distinction (as far as I know) of being the only woman scientist of that time actually to work in the tropics on tropical diseases. She must have been a wonderful character and I wish I had known her.

her publishing an article on a malaria-like parasite of pigeons, a subject that could not excite great controversy or strong passions except amongst a small coterie of purists.

As the bedbug theory being discredited, others were casting about for new candidates. One of the men who was to put his formidable energies to the effort was Major John Sinton of the Central Research Institute's Medical Entomology Section at Kasauli. Sinton, a North Irishman, was to become renowned not only for his stature as a malariologist but also because he would be the only person to hold both of Britain's highest honors, the Victoria Cross for military galantry and Fellowship of the Royal Society for scientific achievement.\textsuperscript{16} At that time, it was not beneath the dignity of physicians to study insects, and most of the foremost medical entomologists were doctors who combined an expertise of medicine and zoology. In considering the kala azar vector problem, Sinton did what any good military man would do: he looked at maps. The map of kala azar showed its restricted range in eastern India, from Madras to Assam. When distribution maps of the blood-sucking biting insects were overlaid on the kala azar map, the range of one species neatly coincided—\textit{Phlebotomus argentipes}, the silvery sandfly. In 1924 and 1925, Sinton published papers advancing his theory that the sandfly was the vector of the kala azar parasite, \textit{Leishmania donovani}. The pursuit of the sandfly was now joined. It would take another twenty years

\textsuperscript{16} During a somewhat careless life in the tropics and elsewhere, I've had several outstandingly frightening experiences—for example, with a hippo who thought I didn't belong in his water, and the confrontational terrors of the African roads. But perhaps the most unnerving experience was, as a very young graduate student, to be the bridge partner of Brigadier John A. Sinton, V.C., F.R.S. "The Brig," a wonderfully kind man, would bid with the same panache that won him his V.C. Mostly three no trump, as I recall. And heaven help his partner who didn't make the contract, no matter what cards he held.
before the final piece of conclusive proof was put into place. But at least the trail was now true.

The Calcutta School of Tropical Medicine had an additional piece of epidemiological evidence incriminating the sandfly—Ward 14. Ward 14 of Calcutta was largely populated by another product of British colonial rule, the Anglo-Indians. Merle Oberon and Ava Gardner’s Bhowani Junction apart, the Anglos led unromantic lives in an ambivalent subculture that was neither quite English nor quite Indian. In expiation for their sins of miscegenation, the parental English virtually bequeathed the Indian railway system upon their mixed-race progeny, and it was run by them with great efficiency. The Anglo-Indians, in making a somewhat distorted cultural alignment, built homes which they thought of as being typical “mother country”—large, morose-looking wooden houses within a compound of thickly shadowing foliage. In 1925, the Anglo-Indians of Ward 14 were dying of kala azar. Their distant Hindu cousins of Calcutta’s northern wards were barely affected by the disease. Searching for the reason for this difference, the Calcutta School of Tropical Medicine scientists headed by Robert Knowles noted that the dark rooms of the Anglo-Indian houses, “lumbered with family furniture,” humid from the surrounding dank vegetation, were optimum conditions for the livelihood of *Phlebotomus argentipes*. The Anglo-Indian houses held large populations of this sandfly, while the simpler, more open shacks and homes of the Indians did not. In the poorer Indian wards there were lots of fleas, lice, and bedbugs, but relatively few sandflies. This finding encouraged the Calcutta School group to begin the demanding transmission experiments.

None of us likes sandflies. They are extremely finicky to breed and maintain in the laboratory. Identification of their species often requires such expert practice as dissecting out their genitalia—and they are very small creatures with very small genitalia. Despite these difficulties, which were even more rigorous in 1925 than now, the Calcutta scientists managed to establish a thriving colony of *Phlebotomus argentipes*. Knowles began to feed these “clean,” laboratory-bred sandflies on kala azar patients; then, day by day, he took the flies apart. On a glass slide under the microscope each fly was carefully dissected and searched for the presence of the flagellate form of *Leishmania donovani*. There was a considerable sense of excitement when these forms were seen in the gut of flies that had been fed on the patients three or four days earlier. Twelve days later the flagellate forms had multiplied and were now in the “throat” of the sandfly. This was great progress, but it still didn’t prove actual transmission. The crucial A to B experiment had yet to be performed: an infected sandfly had to bite a human “guinea pig,” and that human had to come down with kala azar.

The protracted transmission studies were now largely undertaken by officer-scientists deputed to the Indian Kala Azar Commission. The original trio, who set up shop in Assam, were Colonel Rickard (later Sir Rickard) Christophers, Major Henry Edward Shortt (later Professor Shortt), and a Mr. P. J. Barraud whom we don’t hear much of as a “later.” Knowles communicated his findings to the Commission, and Christophers, et al., quickly confirmed the Calcutta group’s findings. Looking into their overly optimistic clouded crystal ball, the Commission predicted in their First Report of 1926 that “Only experimental transmission by the sandfly would therefore now seem to be necessary to prove finally the role of this insect in the transmission of kala azar.” Little did they then know that the
successful A to B experiment would take another fourteen years.

Henry Edward Shortt, the only one of the trio to stay the course, would never carp over what must have been frustrating years. He was a man who pursued, and pursued, his quarry. He loved the hunt. As an Indian Medical Service officer, he shot tiger. As a professor at the University of London’s prestigious School of Tropical Medicine and Hygiene (where he was to discover the missing “liver” link of the malaria parasite’s life cycle), he taught his graduate students, at teatime, how to stalk and kill houseflies by creeping up on them with two extended fingers. As a retired visiting professor emeritus in Africa, he hunted agamid lizards (to study their malaria) with a blowpipe he made from glass laboratory tubing and modeling clay as the pellet missiles. No Jivaro could have been more accurate than this deceptively mild-looking man of modest stature peering at his prey over half-glasses. At the age of one hundred he caught his last trout and died, leaving his widow, his beloved Hobby, to survive him for another year until she joined him in death at age one hundred and three (Knowles had been the best man at their wedding in India those many years ago). Shortt knew that it was now no trick to produce infected flies; but try as he and his colleagues did year after year, time after time, the bite of those flies did not produce infection in human volunteers. Some experimental technique, some trick, was missing. When the trick was finally discovered, it seemed so simple; it also showed how scientists could be snookered for so long behind entrenched, plausible—but erroneous—assumptions.

The assumption was that the sandfly was rather like a small mosquito in its dietary habits. The male mosquito and the male sandfly, gentle souls, are vegetarians, feeding exclusively on fruit juices and other plant material. They partake of no blood. Only the ladies are blood feeders. This is certainly true of mosquitoes but, as it turned out, not quite true of the sandfly. In 1939 a physician-cum-entomologist, Dr. R. O. Smith, established a laboratory in Bihar to study sandflies, beginning the research that was so important in unraveling the transmission knot. First, Smith showed that the female sandfly would readily feed on fruit (Smith gave them raisins) after taking the initial, infecting blood meal. Next, he showed that when the usual procedure was carried out of maintaining the flies on “clean” blood feeds (as in malaria transmission techniques with mosquitoes), the second blood feed would, for some inexplicable reason, halt the multiplication of the flagellate *Leishmania* parasites. It caused them to lose their vitality, and sometimes even wiped them out from the sandfly.

Even more startling was Smith’s observation that the raisin diet following the infective blood meal caused the flagellates to thrive and multiply so enormously that the sheer numbers of organisms formed a plug in the sandfly’s pharynx. It was these “plugged” or “blocked” sandflies that constituted the potential transmissive danger. When they tried to feed again, the plug of parasites occluded the throat and made feeding impossible. The sandflies made violent efforts to ingest blood or other fluids, and in doing so, some of the flagellates of the plug became dislodged. It was these
dislodged organisms that might be capable of infecting a human when the “blocked” sandfly tried to feed. Shortt and all the other researchers had been following the malaria-mosquito experimental procedures of successive blood feeds. With the sandfly *Leishmania donovani*, this gave rise only to non-infective parasites.

In 1940 an Indian physician-scientist, C. S. Swaminath, and Shortt made the successful A to B experiments.\(^{18}\) Swaminath collected six Indian volunteers from a hill district of Assam and fed the “raised” infected flies on them. Three of the volunteers contracted the disease. The sandfly, *Phlebotomus argentipes*, was finally confirmed as the vector of kala azar. Thirty-eight years to prove a point! Only the post-game criticisms customary for new discoveries had still to be dealt with.

There was one bit of sniping that was amusing and would be impossible in modern science’s impersonal, peer-reviewed publication policies. In 1944, a Dr. Malone published a letter in the *Indian Medical Gazette* in which he advanced his doubts that Shortt and Swaminath had proved their case for the sandfly transmission of kala azar. A few weeks later Shortt makes his Shorttian reply in the *Gazette*:

> He knows Dr. Malone to be a disciple of George Bernard Shaw, therefore the opinions of a fervent Shavian socialist cannot be accepted. Finis. At a much later year, Shortt was to refer to a well-known but not-quite-first-class scientist as “The Bishop” because he was always confirming others (including Shortt’s recent discovery of the liver phase of the malaria parasite). Knowles, in his lecture notes from the Calcutta School, sums up the protracted search with a kind of eulogy of exhaustion:

The story of the discovery of how kala azar is transmitted from man to man is one of the most amusing, also perhaps one of the sorriest in tropical medicine. It is a history of almost twenty years of wasted effort, of individual workers starting off with the highest hopes and ending in despair; of false starts and erroneous conclusions; of acute controversies and the flow of much ink; of wasted effort and the absence of co-ordinated enquiry.

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18. From the 1920s onward it was not all a “one-man show” of British scientists; many competent and distinguished Indian physicians were engaged in kala azar research and often took precedence in publication. Shortt always spoke highly of his former Indian colleagues, although he might occasionally grumble that in the midst of a crucial experiment they would depart on a holy pilgrimage for an indeterminate period.