The plague outbreaks of India, 1994 – A prologue

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PLAGUE is a disease of great antiquity in India. India was one of the countries most severely affected by the Third Pandemic of plague which spread around the world through steamships; there were an estimated 12.5 million deaths due to plague between 1886 and 1950 in India[1]. In his autobiography *My World of Preventive Medicine*, C. G. Pandit recollects the night sky of Bombay lit up every night by the rising flames of burning bodies, dead from plague in the early part of this century[2]. From 1950 onwards with the increasing availability of DDT and broad-spectrum antibiotics, plague transmission was gradually curtailed and mortality from the disease much reduced. India's Haffkine Institute played an important role in the history of plague in developing an anti-plague vaccine as early as the turn of the century followed later by treatment trials of patients affected with plague. By 1967, interruption of wild plague transmission to humans appeared to have been achieved in India and human plague outbreaks were no longer reported. Between 1967 and 1993 there were reports of two separate outbreaks of plague but neither of them was confirmed as plague[3]. It is well known that plague cannot be eradicated just as small-pox was and poliomyelitis would hopefully be in the near future. It is a disease of the earth, of the creatures that run and burrow the earth and of the fleas. Man is an accidental victim and need not have plague infection for plague persistence. In recent decades, plague had simply retreated to rural natural foci of infection, involving mostly wild rodents and their fleas with occasional spillovers to commensal hosts and humans in villages and towns[1]. Many natural foci of plague in wild rodents exist today not only in India but throughout the developing world in the continents of Asia, Africa and Latin America. Meanwhile, there had been a shift in plague mortality and morbidity from its dominance in Asia in the 1960s and 1970s to Africa in the 1980s and 1990s with case fatality rates still remaining high.

But epidemics of human plague can be prevented from occurring and controlled with present-day knowledge and methods of surveillance, prevention and treatment. This is what did not happen in India, repeating the usual story of complacency following initial victory against communicable disease[4]. Unstable epizootic factors with hostless fleas are conducive to the outbreaks of human plague.

Thus it was that between August and October, 1994 India was struck by two outbreaks of plague in succession – one of suspected bubonic plague in the Beed District of the State of Maharashtra and the other of suspected pneumonic plague in the Surat city of the State of Gujarat. On the basis of circumstantial and serological evidence the outbreaks were presumed to be plague and they were rapidly brought under control by governmental action at the State level assisted by the Centre. In the process, however, India's vulnerability to emerging and re-emerging infectious diseases was exposed on many counts, especially in the areas of epidemiological monitoring and supportive laboratory services, the essential pre-requisites for rapid response. As the WHO International Team investigating the plague outbreaks in the country said in its Executive Report dated 22 November, 1994, while the outbreaks were raging, there were problems with the investigating laboratories in being able to quickly differentiate real cases of plague from the huge background load of a variety of infectious diseases which also cause epidemics with similar clinical and epidemiological features[5]. 'Diagnosis became overly dependent on procedures that are used to support a diagnosis of suspected plague (Gram stain, Wayson stain of smears prepared from clinical materials). A similar over-reliance was placed on serologic procedures that support a diagnosis of presumptive (probable) plague. (Single serum specimen testing using passive haemagglutination assay)'[5]. May C. Chu, the microbiologist member of the WHO International Team, who comes from the WHO Reference Laboratory for Plague at the CDC in Fort Collins, Colorado, USA, said on November 18, 1994: 'Though there were multiple attempts to isolate *Yersinia pestis* from sputum, blood and autopsy specimens, there is no clearly-identified *Y. pestis* culture associated with any specimen obtained from suspected plague patients.'[6] Thus in those early days, diagnostic uncertainty and confusion prevailed; alternative diagnoses implicating other infectious agents were offered and there was panic and excessive alarm on the part of the public, coupled with widespread reporting by the media. The message

did not go through effectively that in the modern era with its array of insecticides, diagnostic and therapeutic tools, today's plague is not the Black Death of olden times and is readily amenable to prevention and control through a system of surveillance and prompt response. Fifteen airlines cancelled 400 flights to India, resulting in much economic damage.

Against this background, on 9 October, 1994, by which time the two outbreaks had largely subsided, the Government of India constituted the Technical Advisory Committee (TAC)* on Plague with the following Terms of Reference:

1. To elucidate factors responsible for the current outbreak of plague and its spread;
2. To advise on strategies, policies and programmes for the control of plague;
3. To recommend steps for prevention of such outbreaks in future.

TAC initiated work on all the three Terms of Reference but even at the outset it was clear that the on-going controversy in the media and in professional circles as to whether it was plague or not would not abate until conclusive evidence of the identity of the causative agent was found. And unless this was done, TAC could not proceed with addressing its Terms of Reference.

There was, however, a major snag. The outbreaks had largely subsided by the time TAC was formed and so it was not possible for TAC to collect and study fresh material for laboratory confirmation of human plague through isolation of *Y. pestis* from clinical specimens. TAC had to have recourse to the original clinical specimens obtained while the outbreaks were 'on' and stored in Surat and at the National Institute of Communicable Diseases (NICD) in Delhi. The WHO International Team had remarked that attempts at culture isolation and identification of *Y. pestis* at both these places had failed to yield pure characterizable colonies[6]. Contamination of bacterial isolates was a problem. TAC then decided to mobilize the expertise and laboratory facilities available within the country, including those with some members of TAC for this task. Both the new Civil Hospital in Surat and NICD, Delhi, had extended their full cooperation to TAC in providing the stored cultures for TAC's study. The Defence Research and Development Establishment (DRDE) in Gwalior (H. V. Batra) had undertaken the main task of isolation and characterization of *Y. pestis* from the stored cultures and further molecular characterization of the isolates in a pure form was carried out by scientists working in a network of laboratories functioning under various research agencies in India. Scientists in the following institutions played a key role in this effort: the All India Institute of Medical Sciences (AIIMS) (S. K. Panda); the Post-Graduate Institute of Medical Education and Research (PGIMER), Chandigarh (N. K. Ganguly); the Institute of Microbial Technology (IMTECH), Chandigarh (Amit Ghosh); and the Centre for Cellular and Molecular Biology (CCMB), Hyderabad (S. Shivaji). Meetings of the scientists from these institutions were held from time to time and there was a spirit of cooperation and team work amongst them in this endeavour. H. Sharat Chandra of the Indian Institute of Science, Bangalore and a member of TAC coordinated this work. In addition to clinical material from Surat, specimens of original rodent material and of fleas from Surat and Beed collected by NICD scientists during and after the outbreaks were made available to TAC for culture isolation. In the entire work done by TAC and the expert panel to track down the infectious agent, the Health Departments of the State Governments of Maharashtra and Gujarat gave their utmost cooperation.

The result was that *Y. pestis* could be isolated and characterized as such from some of the clinical samples in Surat and from the environmental samples in Beed and Surat. In this issue of *Current Science*, a number of articles appear, narrating the story of isolation and characterization of *Y. pestis* and providing TAC's response to the Terms of Reference. At first there is an overview of the work done by TAC followed by a series of articles on the isolation and characterization of *Y. pestis* from the clinical and environmental samples, the serological evidence, a special article on molecular characterization of *Y. pestis* isolated from the outbreaks, followed by ecological aspects of the outbreaks. These articles are written by scientists who had carried out the work in their laboratories. In the end, the epilogue looks at the future scenario – what next?

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