This Issue

Infectious disease and their causal agents, microbial pathogens, have been with humanity since the beginnings of recorded history. The ravages of contagious disease have diminished with the advance of modern medicine, but there remain many areas of the world, where poverty and poor public health measures leave human populations at great risk from microbial onslaughts. Of the many diseases to which the Indian sub-continent has been home, cholera remains an important health hazard, some regions of the country being particularly susceptible. For long, cholera was indeed the 'scourge of Bengal' and Calcutta its focal point. Researches into the origins of cholera, its mode of transmission, methods of treatment, prevention and control, have been pursued for over a century. A watershed was reached in the late 1880's, with Robert Koch's clear demonstration that the bacterium *Vibrio cholerae* was indeed the infectious agent and that the disease was water borne. Sanitation and public health measures then seemed the way to prevention and control. Koch's work which really marked beginnings of modern bacteriology, did not however, lead to the elucidation of the mechanisms by which *Vibrio cholerae* wreaks its havoc on the human body. Indeed mistaken analogies with diphtheria were to raise a barrier to understanding for a long time to come. This barrier was breached only three quarters of a century later, appropriately enough in Calcutta by Sambhu Nath De, who demonstrated the presence of a cholera exotoxin in culture filtrates of the vibrio.

This issue of *Current Science* seeks to chronicle De's contributions to cholera research, one of the finest chapters of medical and biological sciences in India. Strangely enough, De died in 1985, little known in the Indian scientific community, almost a quarter of a century after the publication of his seminal work. Joshua Lederberg sets the tone for this tribute to S. N. De by pointing out that "our appreciation of De must then extend beyond the humanitarian consequences of his discovery .... he is also an exemplar and inspiration for a boldness of challenge to the established wisdom, a style of thought that should be more aggressively taught by example as well as precept". John Craig notes that De's work "forever altered our concepts surrounding the pathogenesis of secretory diarrhea" and recalls his meeting with De in 1964.

A. Sen and J. K. Sarkar describe De's transition from the village of Garibati to the pathology laboratories of the Nilratan Sircar Medical College and later the Calcutta Medical College. In the span of a decade between 1950 and 1960 De was to make three superb contributions. In 1953 (*J. Pathol. Bacteriol.* LXVI, 559, with D. N. Chatterjee, reprinted in this issue) De devised an animal model for studying cholera, using ligated intestinal loops in rabbits. In 1956 (*J. Pathol. Bacteriol.* LXXI, 201, with K. Bhattacharya and J. K. Sarkar) he was to use this ileal loop model to demonstrate that some strains of the bacterium *E. coli*, do indeed produce a 'cholera like' response. This was the first demonstration of diarrhea producing *E. coli*. Finally, in 1959 (*Nature* 183, 1533, reprinted in this issue) he was to establish that pure, sterile culture filtrates of *Vibrio cholerae* induces fluid accumulation in the intestinal loops, thus establishing the presence of a molecular toxin, which stimulates a specific cellular response.

De's work has had a major impact on the field of cholera research and Eugene Garfield's citation analysis (reprinted in this issue) provides an illuminating view. Historically, De's work was championed by W. E. van Heyningen, whose 1985 article in *Trends in Biochemical Sciences* (reprinted in this issue), really put De's contributions in proper perspective. van Heyningen died in 1989, just before this issue of *Current Science* was planned. He would have surely liked to contribute. We reprint several excerpts from his 1983 book "Cholera. The American Scientific Experience 1947–1980" co-authored with John Seal, and also a brief biographical sketch. Simon van Heyningen presents a personalised view of the field as it has progressed from the discovery of cholera toxin to its molecular mechanism of action.

Thirty years have elapsed since the publication of De's work. How has the knowledge gained from the studies of the toxin helped in development of an effective vaccine. Richard Finkelstein, who first purified and crystallized the protein toxin surveys the area and also points to the importance of work done in the 1950's by N. K. Dutta, then at the Haffkine Institute, Bombay, in the eventual isolation of cholera toxin. Jan Holmgren presents a perspective of the studies leading to an understanding of the toxin structure and discusses prospects of using these results as a springboard for the development of subunit vaccines.

Jyotirmoy Das provides a broad overview of past and present cholera research in India and highlights the major contributions of S. Mukherjee and K. Bhaskaran in addition to those of S. N. De and N. K. Dutta. S. N. Chatterjee summarises research on cholera causing bacilli carried out at the Saha Institute of Nuclear Physics, Calcutta. The current status of diarrheal disease treatment, prevention and control, particularly by oral rehydration therapy is considered by Jan Rohde, S. C. Pal and Hema Viswanathan.

De's work was carried out in relative obscurity in Calcutta, a city which was also the scene of Koch's discovery of the cholera causing comma bacillus over a century ago. An historical section looks back on this event and provides samples of De's correspondence and the unedited text of his last lecture at the 1978 Nobel Symposium in Stockholm.