

SCIENCE AND CULTURE

VOLUME 76 □ MAY-JUNE 2010 □ NOS. 5-6

EDITORIAL

CHOLERA: AN ANCIENT MONSTER KEPT ALIVE BY POVERTY



Cholera is an ancient and perhaps, the most rapidly lethal dehydrating diarrheal disease. The warm and humid Gangetic delta that forms much of West Bengal and Bangladesh of today has nurtured for centuries the organism *Vibrio cholerae* with great care in its ponds, rivers and brackish water at the

confluence of the numerous tributaries of the Ganga with the Bay of Bengal and has been infamous as the homeland of cholera. As recently as the early 20th century, the disease caused millions of deaths in dense human clusters in the fertile plains of India almost every year and we find moving imprints of the consequent human misery in the contemporary literature. In its most severe manifestation, often referred to as *cholera gravis* or *Asiatic cholera* caused by the now extinct classical biotype of *V. cholerae*, the patient died within 4 hr of the first rice-water stool. In fact, an epidemic of classical cholera resembled more a natural disaster like a tsunami or a severe cyclone than a typical infectious disease in its devastating effect on society. Although the disease had its epicenter almost always in India, it had its presence in all the five continents of the globe till the end of the 19th century. Cholera, now almost synonymous with poverty and destitution and restricted to developing countries with poor sanitation and public health facilities, had many distinguished victims in the past. The discoverer of the second law of thermodynamics, Sadi Carnot, the French novelist Alexander Dumas, the great German idealist philosopher Hegel, a President of the United States of America, James K. Polk, the Irish philanthropist and a leading light of the Bengal Renaissance, David Hare were all victims of cholera. It is, therefore, no wonder that it engaged the attention of the greatest microbiologists of

the 19th century like Robert Koch, who discovered the causative organism, *V. cholerae* in 1884 and Louis Pasteur, who toyed with the idea of attenuating virulence for vaccination by immunizing humans with chicken cholera vibrios for protection against cholera in 1880.

The ferocity of cholera abated somewhat with the gradual replacement of the classical biotype of *V. cholerae* by the less virulent El Tor biotype in the early 1960s. The change in biotype toward the less virulent phenotype was something natural in the evolution of microorganisms and seems to be related to better adaptation of the El Tor biotype with the environment. Successful implementation of the oral rehydration therapy, which involves replenishing water and electrolytes purged out in the severe diarrhea, was a real breakthrough in the clinical management of the disease and reduced the mortality of cholera drastically from about 50% to less than 1%. Still, millions of people continue to suffer from the disease, especially in the aftermath of a natural calamity like a flood or earthquake or of some events like wars or political unrests leading to migration of humans on a massive scale like the one seen during the Bangladesh war of liberation in 1971. Even under normal circumstances, the burden of cholera is steadily increasing in our country, as shown by a recent publication in the WHO Bulletin [Kanungo et al. Vol. 88, 185, 2010]. The average disease burden in India is around 3 to 5 million cases with 100 000 to 130 000 deaths. Since *V. cholerae* is a normal inhabitant of our aquatic environment, elimination of the organism is not a realizable dream either for India or for a nation with the wealth or scientific resource of the USA. However, the USA and Europe have eradicated cholera without eliminating *V. cholerae* from the environment and we in the developing countries have miserably failed to do so. The reasons are not far to seek. Cholera, as it stands at the beginning of the 21st century, is basically a socio-economic problem. It is a price we have to pay for living in overpopulated, squalid slums with little or no access to clean water. It is also a price for bringing up our children malnourished, illiterate and

unaware of the rudiments of hygienic practices. This is a disease where science has its grave limitations in alleviating human suffering.

Perhaps, it is only natural that any deliberation on cholera evokes morbid images of emaciated children with death staring at their faces thronging at the outdoors of city hospitals. But no human misery is an unmixed curse. Cancer has caused excruciating pain and death to its victim but has also taught us the wonderful details of cellular development and differentiation processes, much of which would have otherwise remained unrevealed. Research in cholera has contributed enormously to our understanding of bacterial evolution, mucosal immunity and signal transduction pathways in eukaryotic cells. It is a matter of great pride for Indian scientists that the modern era in diarrheal disease research started with the discovery of cholera toxin by Sambhu Nath De in Kolkata in 1959 in an animal model developed by him a few years earlier. Previously, it was generally thought that the clinical symptoms of cholera are caused by some somatic component of the bacterial cell wall like endotoxin or lipopolysaccharide and it was De who first showed that virtually all clinical symptoms of cholera are caused by a single extracellular protein. This small but fundamental work of De spawned several thousand publications in the area in the next few decades.

Strange it may sound, but it is a fact of science that pathogenic microorganisms have a strong predilection for the less privileged in the society. People in the developed countries rarely suffer from diseases like diarrhea, tuberculosis, malaria and leishmaniasis. Yet, these are the

diseases that are the most important contributors to death and misery of more than two-third of the humanity living in the less fortunate countries of Asia, Africa and Latin America. Because the victims are less articulate than the more affluent, the mute suffering and pain of these people tend to be glossed over by the scientific leadership in the developed countries. We thank the Editorial Board of the **Science and Culture** for giving us an opportunity to deliberate on cholera, a disease which no longer enjoys the glare of attention of the modern biomedical science.

In the first article of this issue, Prof. Yoshifumi Takeda has summarized more than 100 years of research on cholera with reminiscences of his deep association with the problem. T. Ramamurthy and G. B. Nair have discussed the genetic mechanism of evolution of *V. cholerae* to explain the emergence of strains with altered virulence pattern, K. K. Banerjee has described how the molecular approach to the study of the modes of action of cholera toxin and *V. cholerae* hemolysin have contributed to our understanding of pathogenesis of cholera in particular and to signal transduction pathways and protein movement across biological membranes in general. Prof. A. C. Ghose has summed up the 100 years of hope and frustration in developing an effective cholera vaccine.

Finally, we wish to express our sincere gratitude to Prof. S. C. Roy for his patience and cooperation that has made this issue possible. □

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Guest Editors

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Dr. G. Balakrish Nair is Director of the National Institute of Cholera and Enteric Diseases, Kolkata. He is an eminent microbiologist, who has made many outstanding contributions in areas of Clinical Microbiology and Molecular Epidemiology with emphasis on *Vibrio cholerae*. He was awarded the *Shanti Swarup Bhatnagar* award for medical science in 1998 in recognition of his contribution toward the discovery of a new epidemic serogroup of *V. cholerae*, globally known as *V. cholerae* O139. He is a Fellow of the National Academy of Sciences, India, a Fellow of the Indian National Academy of Sciences and a Foreign Associate of the National Academy of Sciences, USA.

Editor's Note : This special issue has been sponsored in part by the National Institute of Cholera and Enteric Diseases at Kolkata.